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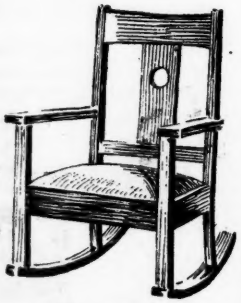

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FAMILIAL HÆMOLYTIC SPLENOMEGALY.[1]

BY S. O. COWEN, M.D. (MELBOURNE),

Acting Physician to Out-Patients, Melbourne Hospital; Clinical Research Scholar, Melbourne University.

THE object of this paper is to record the investigation of a remarkable series of cases of enlargement of the spleen associated with anæmia and jaundice occurring in one family.

My interest in the subject was first aroused in December, 1920, when a young man, aged twenty-three, presented himself in the Out-Patient Department of the Melbourne Hospital complaining of lassitude and weakness with intermittent pain in the lower region of the chest on the left side. He was slightly jaundiced and examination revealed an enlarged spleen, the discovery of which prompted him to remark that there was spleen trouble in the family and that his father was also under treatment in one of the wards for a similar condition. Further inquiry disclosed the fact that they were members of a family well known to the more senior members of the staff since its discovery by Dr. J. W. Springthorpe twenty years ago. The results of his detailed and painstaking observations were first published in 1904,[1] when the histories of six affected members were set out, together with an account of two successful splenectomies performed by Mr. R. A. Stirling. That these operations were amongst the earliest deliberately performed for enlargement of the spleen should be placed on record as a tribute to their pioneer work. In 1908 Dr. Springthorpe[2] recorded the subsequent history of the patients and noted the remarkable improvement in those whose spleens had been removed. Naturally this familial group of cases aroused great interest both here and abroad. They are referred to in every publication of importance concerned with diseases of the spleen, but doubt is frequently expressed as to their true nature. Though Dr. Springthorpe quite rightly regarded them as belonging to the group of diseases known as idiopathic splenomegaly, the term splenic anæmia which he applied to them, can no longer be considered correct. The interest aroused by the simultaneous reappearance of the two patients referred to above prompted me, therefore, to continue the investigation begun by Dr. Springthorpe and to review the diagnosis in the light of recent additions to our knowledge.

The Clinical Material.

Since 1908 the family has multiplied considerably and the total number of members is now forty-eight,

[1] Read in abstract at a meeting of the Victorian Branch of the British Medical Association on October 4, 1922.

spread over three generations. Many new cases have arisen and some of the patients have been under treatment in the Melbourne and Children's Hospitals. Information concerning twelve members has been obtained from Dr. Springthorpe's papers and from the hospital records. Five of the original patients have been re-examined, including two whose spleens were removed. Fourteen others have been examined. Of the twenty-six whose condition has thus been ascertained, fourteen were found to be affected with the family disease, while three others, now dead, whose records are too meagre to justify a positive diagnosis, were probably affected. The family tree is shown diagrammatically in Figure I.. It is regretted that the investigation is incomplete, but the family is widely scattered about Victoria and, though most of the accessible members have readily submitted to examination, a few have refused to do so. Treatment has been carried out in a number of patients whose condition required it and the results observed.

The clinical data so obtained have been reviewed in the light of a survey of the available literature on splenic diseases. The conclusion reached is that these cases should be classed as examples of familial hæmolytic splenomegaly. A summary of the facts observed and the deductions therefrom on which this opinion is based, is here presented. A critical review of the enormous literature has not been attempted, references being given only to publications which have been directly utilized in the preparation of this paper. At the outset I wish to express my indebtedness to the work of Pearce and his collaborators.[3] Their book, "The Spleen and Anæmia," is not only a record of accurate experimental work, but also contains a valuable summary of the clinical features of splenic diseases and a full bibliography.

I wish gratefully to acknowledge the assistance afforded to me in this inquiry by the Clinical Research Committee of the Melbourne University.

The Evolution of the Conception of Hæmolytic Splenomegaly.

The clinical observations which follow, will be rendered more intelligible by indicating briefly the successive steps which led to the differentiation of hæmolytic splenomegaly and the characteristics which distinguish it from other members of the group of diseases known as idiopathic or primitive splenomegaly. This group embraces several distinct clinical entities and a number of less clearly defined conditions. In all of these the splenic enlargement, though not strictly primary, is the predominating feature and is not associated either with a general infective disease or with a disturbance of other organs of the hæmopoietic system.

Idiopathic splenomegaly may be said to have come into being in 1832 when Hodgkin[4] described seven cases presenting enlargement of the spleen and lymph glands dependent on several different causes. The cases of leuchæmia reported in 1845 by Bennett[5] and Virchow[6] established the identity of that disease and brought under general notice the close connexion between splenic enlargement and increase in the number of white corpuscles in the circulating blood. During the following year several observers reported cases of enlargement of lymph glands and spleen with many of the clinical features of leuchæmia, but without increase of leucocytes. This group received various names, of which "pseudo-leuchæmia," applied to it by Cohnheim, was most generally adopted. It included the most diverse diseases, but gradually it was divided into sub-groups, of which only splenic pseudo-leuchæmia or primitive splenomegaly, denoting condi-

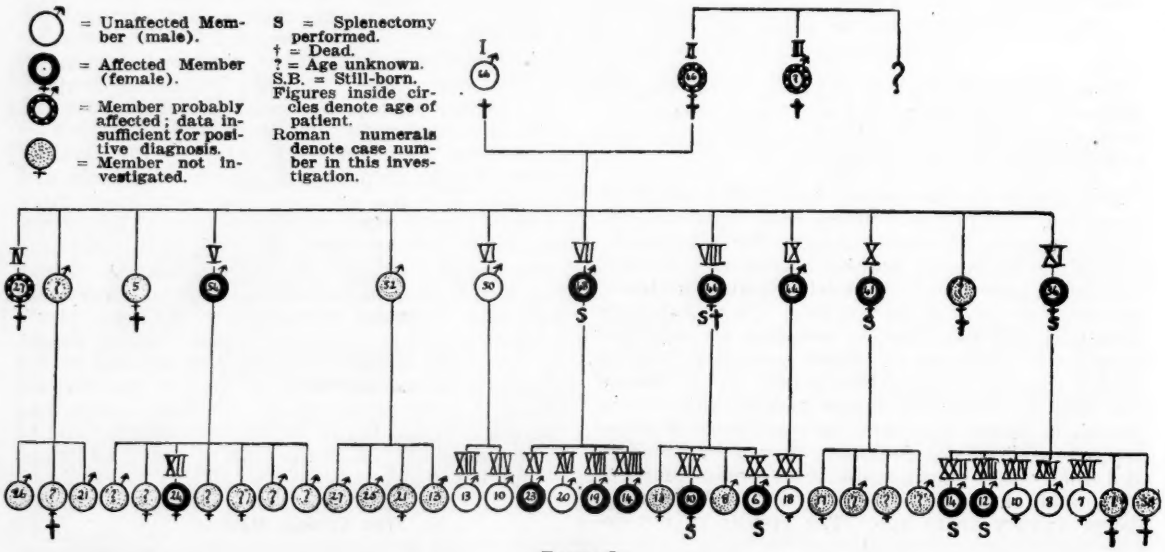
= Unaffected Member (male).
= Affected Member (female).
= Member probably affected; data insufficient for positive diagnosis.
= Member not investigated.
S = Splenectomy performed.
† = Dead.
? = Age unknown.
S.B. = Still-born.
Figures inside circles denote age of patient.
Roman numerals denote case number in this investigation.

FIGURE I.
The Family Tree.

tions in which the spleen is enlarged, but not the lymph glands, directly concerns us here.

Of the several diseases denoted by this term, splenic anæmia was the first to be clearly defined. Sippy,[7] in his excellent historical summary, states that, though Gretzel described a case in 1866, it was Banti's description in 1883 that established the condition as a clinical entity. Osler[8] in 1900 gave the first comprehensive account in English of splenic anæmia and described the characteristic symptoms: Splenic enlargement, a tendency to hæmorrhages, especially hæmatemesis, anæmia of moderate degree without much evidence of bone marrow activity, leucopenia and, in the later stages, ascites and jaundice. More recent investigations enable us to add that the corpuscular fragility is unaltered or decreased; that there is no evidence of excessive hæmolysis and that no familial incidence is found. The pathological features are fibrosis of the spleen and, later, cirrhosis of the liver. Splenectomy, which was at first considered curative,[9] can in the light of the after history of the cases[10] only be regarded as palliative. The present tendency is to regard splenic anæmia not as a specific disease, but rather as a symptom complex consequent on fibrosis of the spleen due to local or general infections of different kinds.[11] In this way syphilis may produce a picture identical with Banti's disease.[12]

Gaucher in 1882 described a case which clinically resembled splenic anæmia, but differed from it markedly in its pathological features. Brill and Mandelbaum[13] in 1913 collected a number of similar cases and their paper may be said to have definitely established Gaucher's disease as a separate entity. Not only does the pathology differ from that of splenic anæmia, but there is a distinct familial tendency. The corpuscular fragility is normal and excessive hæmolysis does not occur. Splenectomy does not cure the disease.

Even after separating off these two clearly defined conditions from the idiopathic splenomegaly group, many obscure cases remain. Certain of these present varying degrees of hepatic or splenic enlargement associated with jaundice. French observers have multiplied types and named them according as enlargement of one or other organ predominates. Much confusion has resulted, but from it emerge two distinct types of disease. At one extreme lies hypertrophic biliary cirrhosis, in which the increase in size of the liver greatly exceeds that of the spleen, while the jaundice is of hepatic origin and there is no increase in the corpuscular fragility. Hæmolytic or acholuric jaundice stands in direct contrast in that the splenic enlargement predominates and the jaundice is dependent on excessive destruction of unduly fragile red corpuscles. This latter factor is also instrumental in producing a marked anæmia. Between these two extremes lies a number of indefinite cases, the variations in their symptoms not permitting their classification under either heading. Hæmolytic jaundice, therefore, is not capable of final definition and is to be regarded as a tentative grouping of allied cases rather than a single specific disease. Nevertheless, it has sufficient clinical meaning to be of practical value. It occurs in both acquired and familial form, the latter being exemplified by the cases under review.

The General Clinical Features.

This paper is based upon the examination of nineteen members of the family, but it would be beyond its scope to consider their several clinical histories in detail. Summaries of the histories of two affected members—one adult and one child—must suffice to illustrate the general features of the clinical picture. These will afford a definite basis for the subsequent discussion of the nature and significance of the more important symptoms.

Case Histories.

CASE XX., male, *ætatis* one year and four months, was admitted to the Children's Hospital, Melbourne, on October 3, 1916, with the diagnosis: "Splenic anæmia, bronchopneumonia right base." The mother stated that the child had always been sallow and bloodless and that she had been able to feel his spleen since birth. From the notes of the examination it appears that the patient was a yellow baby with pale lips; its spleen was greatly enlarged. The blood contained 1,800,000 red blood corpuscles and 28,000 white blood corpuscles to the cubic millimetre. The hæmoglobin value was 35%. There was evidence of severe anæmia of a secondary type; a few nucleated red cells were present. The leucocytes did not manifest any distinctive abnormal features. There were signs of extensive consolidation at the base of the right lung, but the child recovered and was discharged six weeks later.

He was again admitted on April 19, 1921, when five years and ten months of age, the mother stating that his spleen had been getting noticeably larger during the previous twelve months. He had no pain, but got cross and seemed to lose the use of his legs about once a week. Otherwise he was very lively. He was very constipated and had no vomiting. His urine was very discoloured, dark at first and becoming pink and milky on standing. From the notes it is gathered that the child had a sallow complexion; the conjunctivæ were slightly jaundiced; the subcutaneous fat was well preserved. The pulse rate was 96, the temperature was 36.5° C. (97.8° F.). The spleen was much enlarged, the notched anterior border extending to the umbilicus. The lower edge of the liver reached to one finger's breadth below the costal margin. There was no ascites. There was no enlargement of the superficial glands. The heart, lungs and nervous system appeared normal. The urine contained no albumin, no sugar and no bile; urobilin was present in considerable excess. Urates stained pink with uroerythrin were present in large quantities. The Wassermann test failed to yield a reaction. The red blood corpuscles numbered 3,040,000 per cubic millimetre, the white blood corpuscles 13,100; the hæmoglobin value was 50%; the colour index was 0.8. The differential count of the leucocytes was within normal limits. There was gross anisocytosis and poikilocytosis of the erythrocyte and some megalocytes. Polychromasia was a marked feature. A few stippled red cells, numerous nucleated forms, eight normoblasts and thirteen megaloblasts were noted in counting three hundred white cells.

The corpuscular fragility was above normal, hæmolysis occurring in 0.525% solution of sodium chloride. The coagulation time was four minutes.

The blood serum was yellow and gave a strong reaction to Gmelin's test for bile.

The child was kept in bed in the open air and given plenty of nourishing food, but no medical treatment was ordered. A fortnight later there was considerable improvement and the jaundice was much less, but the child was listless and preferred to lie in bed rather than to run about. The red cell count had risen to 4,460,000 per cubic millimetre and the hæmoglobin value to 68%; the colour

index was 0.75, but stippled red cells, megaloblasts and normoblasts were still numerous (see Figure II.).

Splenectomy was performed by Dr. H. D. Stephens on May 2, 1921; the operation was well borne.

Convalescence was rapid and by May 20, 1921, the child was much more active and bright than before the operation and seemed practically normal. The blood examination showed 4,560,000 red blood corpuscles, a hæmoglobin value of 80% and a colour index of 0.9. The inequality of shape and size of the red cells was much less marked; polychromasia was absent and only one normoblast was seen in counting three hundred white cells. The fragility of the red cells remained at the same level as before operation, but the yellow tint of the serum had disappeared and no bile reaction was obtained on applying Gmelin's test.

He was discharged from hospital on May 20, 1921.

CASE IX., male, *ætatis* 44, was seen on February 17, 1921. The history was that he always had a sallow complexion and his eyes had been "yellowish" as long as he could remember, the tint varying from time to time. He had felt perfectly well until two years before, except that for many years he had suffered from obstinate constipation. About two years ago he began to feel weak and tired; these symptoms varied in intensity, so that he described himself as having "ups and downs," each of a few days' duration. During the exacerbations of symptoms his sallowness became more marked and he experienced twinges of pain in the left upper segment of his abdomen and in the gall bladder area. He had not had attacks of vomiting. There had been no hæmorrhages under the mucous membranes or skin.

On examination he was found to be stout, with well marked deposit of subcutaneous fat in the abdominal walls. His skin was sallow, but not definitely jaundiced. The conjunctivæ were distinctly jaundiced and showed yellow thickenings of fatty appearance, triangular in shape, with the bases at the corneal margin and the apices running towards the inner and outer canthi. The spleen was very large, its notched anterior border extending to the umbilicus; its surface was smooth and it moved very little with respiration. The smooth edge of the liver could be felt two fingers' breadth below the costal margin. There was no sign of free fluid in the peritoneal cavity. Examination of the heart, lungs and nervous system revealed nothing abnormal. There was no enlargement of any of the lymphatic glands. The pulse rate was 88. The temperature was 36.8° C. (98.2° F.). The urine was of very dark colour; its specific gravity was 1,020. It was acid and contained no albumin and no sugar; it contained considerable quantities of bile. Urobilin was present in excess of normal quantity. The Wassermann test did not yield a response. The result of the blood examination was as follows:

Red Blood Corpuscles	3,062,000
Hæmoglobin	74%
Colour Index	1.2
White Blood Corpuscles	9,266
Poly-morpho-nuclear Neutrophile Cells	66%
Small Lymphocytes	8%
Large Lymphocytes	9%
Large Mononuclear Cells	4%
Transitional Cells	7%
Eosinophile (poly-morpho-nuclear) Cells	5%
Myelocytes	1%

There was moderate anisocytosis and poikilocytosis. Some macrocytes were seen. Polychromasia was frequent. There were numerous stippled red cells. One normoblast was detected.

The colour of the blood serum was bright yellow. There was a reaction to Gmelin's test for bile. Spectroscopic examination showed well-marked urobilin bands.

Corpuscular fragility was greatly increased, hæmolysis commencing at a dilution of 0.6% sodium chloride.

On May 21, 1921, the patient said that he felt better. His colour was improved, but his conjunctivæ were still slightly jaundiced. The urine was dark brown; its specific gravity was 1,018; its reaction was acid; it contained neither albumin nor sugar nor bile; urobilin was present in great excess. Blood examination showed little change, except that the red cells had fallen to 2,570,000 with a colour index of 1.3.

On June 12, 1921, the patient stated that he felt well and was in one of his "ups." His colour was almost normal; his conjunctivæ were still slightly jaundiced. The spleen was as before. The result of the blood examination was as follows:

Red Blood Corpuscles	3,510,000
Hæmoglobin	82%
Colour Index	1.2
White Blood Corpuscles	14,900

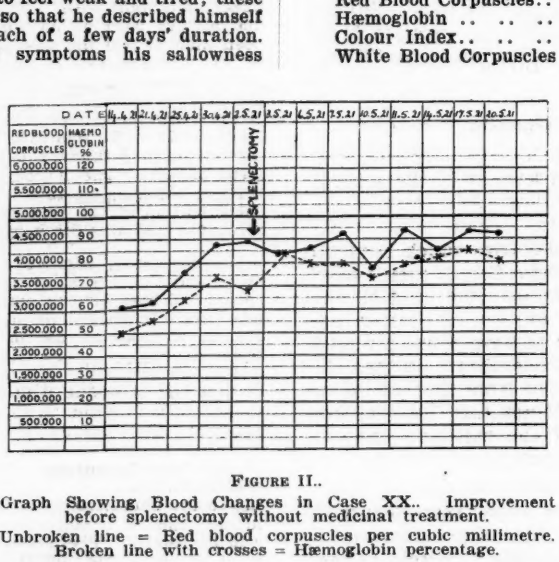

FIGURE II..

Graph Showing Blood Changes in Case XX.. Improvement before splenectomy without medicinal treatment.

Unbroken line = Red blood corpuscles per cubic millimetre.
Broken line with crosses = Hæmoglobin percentage.

The differential count was as follows: Polymorpho-nuclear cells, 63%; small lymphocytes, 7%; large lymphocytes, 9%; large mononuclear cells, 8%; transitional cells, 5%; eosinophile (poly-morpho-nuclear) cells, 4%; poly-morpho-nuclear mast cells, 2%; myelocytes, 2%.

Anisocytosis was definite, chiefly small forms, but there were some macrocytes. Polychromasia was infrequent. No stippled red cells were seen. One normoblast was noted.

The urine contained no bile, but urobilin in excess. The serum was distinctly yellow; bile was demonstrated by Gmelin's test. The corpuscular fragility was unchanged.

The possibility of splenectomy was discussed, but the patient would not entertain the idea. Arrangements were made for application of X-rays to the spleen, but for some unknown reason this was not carried out.

This patient is the father of an unaffected child (No. XXI.).

Both these patients present the features of an advanced stage of the disease; the majority of the members of the family are at present more mildly affected. The case histories detailed are not, therefore, typical, but they have been selected as giving a clear-cut picture of the main symptoms. Common to both are splenomegaly, anæmia, increased corpuscular fragility and jaundice. The age of onset, however, appears to differ considerably in the two patients. The nature and significance of these features must now be discussed in detail.

The Age of Onset.

In its earlier stages the manifestations of the disease are slight and for some time, years may be, the patient perceives nothing amiss. Then gradually there appear symptoms referable to the anæmia,

tiredness, disinclination for exertion and sometimes shortness of breath. At the same time or soon after jaundice and splenic enlargement may be noticed. So insidious are the onset and progress of the symptoms that it is impossible to determine even approximately the age at which they commence. Their first appearance can be more or less accurately dated in only eight cases. In these it was said to have occurred at forty-five, forty-two, nineteen, thirteen, twelve, twelve, eleven and seven years of age respectively. In one instance a child was said to have been affected at birth. The age of affected members in whom no symptoms had been noted, was thirty, nineteen, in three instances ten years.

These variations cannot be ascribed to differences in environment and nourishment or other factors which might be thought to favour the development of anæmia, since the symptoms appear at different ages in children living under exactly the same conditions. There is no evidence that acute or chronic infections light up the symptoms and in no instance has their appearance followed any acute illness. The factors at work will be further considered in discussing the pathogenesis.

The Splenic Enlargement.

Enlargement of the spleen is a constant feature and its degree varies with the severity of the general symptoms of anæmia and debility. Where these are slight, as in Case XVIII., the organ may not be palpable, but percussion demonstrates a definite increase in the area of splenic dulness. In three children with more advanced symptoms the notched anterior border could be felt at or just below the costal margin, whilst in the most gravely affected child it reached to the umbilicus; in all the general symptoms were severe. The enlargement is therefore never very great. These clinical findings are confirmed by the weights of the spleens removed, which do not reach a high figure.

The children sometimes complained of pain over the area of the spleen, but the organ always moved freely with respiration. In the adults, pain was much more constant and severe and the spleen was practically immobile. This suggests the occurrence of a peri-splenitis, the existence of which was actually demonstrated at operation.

The spleen, therefore, enlarges early and increases in size *pari passu* with the progress of the disease. The enlargement is never extreme; it is generally less than in splenic anæmia and does not approach the huge dimensions found in Gaucher's splenomegaly.

The Anæmia.

The general features of the anæmia are illustrated by the results of the blood examinations in the two cases detailed above. Certain points, however, require further elucidation.

The decrease in number of the red cells varied within wide limits, but was never extreme. It may be illustrated by the counts made when the patients first came under observation. In seven adults the average was 3,230,000 per cubic millimetre, the highest being 4,912,000 and the lowest 2,250,000. In seven children the average was 3,570,000, the counts ranging from 4,600,000 to 1,800,000. The lower figures in both adults and children were the lowest obtained at any stage of the disease. The average of one hundred and three cases collected from the literature by Krumbhaar[3] was 3,340,000. These figures are to be interpreted very broadly, since remarkable fluctuations occur without obvious cause. Moreover, the anæmia is dependent on factors of environment as well as on the familial disease. In Case XX., a child living under very poor conditions, marked improvement followed admission to hospital. No drugs were given, but the child was kept clean and adequately clothed and given abundance of nourishing food (see Figure II.).

The hæmoglobin generally showed a comparatively lower figure than the red cells. The colour index was therefore usually under 1, varying from 0.7 to 0.8. In some of the long-standing cases in adults it was slightly above normal, reaching as high as 1.3 in Case IX.. In every instance improvement in the general condition and increase in the number of red cells was accompanied by a lowering of the colour index, suggesting that the outstanding feature of the anæmia is a diminution in the number of cells rather than a deficiency of hæmoglobin.

The degree of abnormality of the red cells, as seen in stained films, bore an almost constant ratio to the severity of the general features of the disease. In the mild cases well-marked anisocytosis was seen with but little poikilocytosis, frequent polychromasia, a few stippled red cells and an occasional normoblast. The majority of the red blood corpuscles were small and large forms were infrequent. Red cells of bizarre shape were constantly present in small numbers, but could not be said to form a striking feature of the films. In the more severely affected children the film showed greater abnormality, as illustrated by the following count of Case XX.:

Red Blood Corpuscles	3,760,000
Hæmoglobin	64%
Colour Index	0.85

The red cells revealed gross inequality in size and shape; some large forms were noted. There was well defined polychromasia, while a few stippled red cells, sixteen normoblasts and fourteen megaloblasts were noted in counting three hundred leucocytes.

As regards the abnormality of the red cells and the number of nucleated forms, this was the worst blood examination of the whole series.

These findings serve to illustrate the profound disturbance of the erythrogenetic apparatus. It is to be noted that regenerative forms, *e.g.*, polychromasic and nucleated cells, predominated over degenerative forms, such as red cells of bizarre shape. The significance of stippled red cells is debatable; it has lately been asserted that they are regenerative forms.[14] Stress has been laid, particularly by American workers, on the presence of reticulated red cells as evidence of active erythrogenesis. They are regarded as immature, hastily produced cells and can be demonstrated only by vital staining. The most commonly used dye for this purpose is brilliant green, which I was not able to obtain. Late in the course of these investigations my attention was drawn to the work of Buckman and Hallisey,[15]

who recommend the use of cresyl violet. Following their technique, the presence of reticulated red cells was found to be a constant feature in two cases.

The blood in the affected adults showed similar changes in the red cells, but the colour index was often over one. Megalocytes appeared in larger number than in the children, but nucleated and polychromasic red cells were fewer.

No very striking or constant variations in the number of leucocytes were found. The count was, as a rule, higher in children than in adults. In three cases of varying severity in children nineteen counts before operation averaged 15,000, ranging from 8,000 to 24,000, while in two adults, both grossly affected, the range was from 5,100 to 14,900, with an average of 7,600. Though the whole count tends to fall in the older patients, a true leucopenia, like that found in splenic anæmia, does not occur.

In the milder cases repeated counts showed no abnormal white forms except a small percentage of poly-morpho-nuclear neutrophile cells with an "elementary" type of nucleus. In the more advanced, however, neutrophile myelocytes were a constant feature. They formed from 0.3% to 2% of the total white count, 4% being the highest figure recorded. As might be expected, they were most numerous when the red cell changes evidenced marked activity of the bone marrow. Eosinophilia did not occur, nor did the lymphocytes, large mononuclear or transitional forms show any alteration of proportion as regards each other or the total leucocyte count.

The blood findings may be summarized as follows: Anæmia is a constant feature. In the milder cases it is not intense; the colour index is under one and evidence of active erythrogenesis is always present, though not in striking degree. As the disease progresses the red cell count becomes lower and the colour index rises, sometimes reaching a figure over one, and the film gives evidence of considerable activity of the bone marrow, especially as regards its erythrogenetic function. Still later, however, in the long-standing cases in adults, the decrease in the total leucocyte count and in the number of nucleated red cells indicates that the marrow activity lessens. Probably this is an expression of exhaustion after long continued over-stimulation; if it were due to any direct toxic effect on the bone marrow it would probably occur earlier.

Especially when the colour index is over one, the blood picture strongly resembles that of pernicious anæmia. One of the earlier patients was, in fact, discharged after investigation with the diagnosis of splenomegaly; anæmia of pernicious type. The reason for this similarity is that certain fundamental factors in the production of anæmia are common to both pernicious anæmia and hæmolytic splenomegaly. The relationship of the two will be again referred to.

The Corpuscular Fragility.

The red cells of the affected members of this family show greatly diminished resistance of hypotonic saline solutions. The degree of increased fragility can be measured by mixing equal quantities of blood with constant volumes of different dilutions of sodium chloride solution. Erythrocytes can remain in isotonic saline solution for some hours without damage, but are quickly hæmolysed by distilled water, the hæmoglobin being "laked" out of the corpuscular stroma. By selecting suitable intermediate dilutions of saline, the points at which hæmolysis commences and at which the corpuscles are completely laked, can be determined.

The actual technique of the test has been varied by different observers. The method used in this series is a modification of Butler's,[16] so designed that it may be carried out at the bedside without any special apparatus. The details are as follows: Twelve small test tubes, such as are used for collecting blood for Wassermann tests, are sterilized by dry heat and placed in a row in a suitable rack. In them are placed dilutions of saline commencing at the left hand end with 0.375% and increasing in each tube by 0.025% up to 0.65% in the twelfth tube. The dilutions are made with distilled water and a 1% saline solution, which keeps indefinitely in a well stoppered bottle. A small glass hypodermic syringe is used as a dropping pipette and the quantities so regulated that each tube contains forty drops of the required dilution. The correct amount of 1% saline solution, *e.g.*, twenty drops for the 0.5% solution, twenty-four for the 0.6% solution and so on is measured into each tube. The syringe is then washed several times in distilled water and the amount of the latter required to complete the necessary dilution in a volume of forty drops is added to each tube. The same syringe is then boiled, washed in sterile normal saline solution and used for withdrawing blood from a suitable vein. The first syringeful of blood is rejected, the needle being left *in situ*. When the barrel is filled for the second time the needle is withdrawn with the syringe and four drops of blood are measured into each tube of saline solution. The contents of the tubes are mixed by gentle shaking and they are then allowed to stand at room temperature and the results noted at any time from three to six hours later. In those containing the lower dilutions complete hæmolysis may occur, whilst in the upper part of the series the corpuscles will sink to the bottom, leaving clear, untinted saline solution above. At some intermediate point a tube will be found in which the supernatant saline solution shows a faint pink tint due to slight hæmolysis, whilst the next higher dilution shows no trace of colour above the sedimented corpuscles. This end point is always clearly marked. It has been used throughout this series as indicating the degree of increase in the corpuscular fragility.

That this technique is sufficiently accurate for clinical purposes is shown by the fact that a long series of observations of normal blood used as a control always gave the same reading. Furthermore, in three cases the results were the same as those obtained by using a capillary pipette. Its chief advantage lies in the readiness with which it may be performed without special apparatus. If necessary, the tubes can be centrifuged instead of waiting for the corpuscles to sediment. The chief fallacy, one common to all methods in which whole blood is used, is that the colour of a highly jaundiced

plasma may simulate the tint of slight hæmolysis and obscure the end point.

The dilutions at which hæmolysis commences and at which it is complete, roughly parallel one another in different cases. The point at which laking is complete, depends, however, on the respective amounts of blood and saline solution used. The findings of different observers as to this point vary, therefore, according to the technique adopted. For this reason the figure at which hæmolysis commences, is more constant and reliable and has been adopted as the measure of the degree of increase in the corpuscular fragility in these cases. The results are incorporated in the following tables, a normal control and a case of splenic anæmia being added for the sake of comparison:

A.—Affected Members (Before Splenectomy) and Controls.

Case.	Percentage Dilution of NaCl at which Hæmolysis Commenced.
Normal Control ..	0.425 (repeated tests)
Splenic Anæmia ..	0.4
IX.	0.575
XII.	0.575
XVII.	0.475
XVIII.	0.5
XIX.	0.5
XX.	0.55
XXII.	0.525
XXIII.	0.6

B.—Affected Members Not Investigated Until After Splenectomy.

Case.	Percentage Dilution of NaCl at which Hæmolysis Commenced.
VII.	0.525
VIII.	0.5
XI.	0.5

C.—Unaffected Members.

Case.	Percentage Dilution of NaCl at which Hæmolysis Commenced.
XVI.	0.425
XXI.	0.425
XXV.	0.425

Chauffard[17] in 1908 first noted the increased fragility of the red cells in cases of acholuric jaundice. His findings have been abundantly confirmed by subsequent observers, but a few cases have been recorded which presented the general clinical features of hæmolytic splenomegaly associated with normally resistant corpuscles. Despite these apparent exceptions, it may be stated that increased fragility is an essential feature of the disease. Its importance may be illustrated by reference to Case XVIII., male, *ætatis* fourteen years, who complained of weakness and general ill-health. Though clinical examination failed to reveal splenic enlargement and jaundice and only slight anæmia was present, the occurrence of hæmolysis in 0.5% of saline solution established the fact that he was suffering from the family disease. It may be added that chemical evidence of jaundice was found in his blood serum.

As a rule the more severely affected patients showed higher fragility figures than those with milder manifestations. This generalization, however, is by no means absolute. It is, as yet, impossible to state whether the figure in any given case is a permanent one or whether it progresses with age and increasing severity of symptoms. Until this point has been decided, the minor variations in the results in members of this family cannot be more fully explained.

It has been suggested that the corpuscular fragility may be due to the action of some substance in the plasma. Butler[16] and others, however, have shown that the findings differ very little when washed red corpuscles are used instead of whole blood. Pearce,[3] too, states that the work in his laboratory and elsewhere has tended to show that the change is in the cells themselves.

The effect of splenectomy on the fragility will be considered later.

The Evidence of Hæmolysis.

The chief manifestations of excessive hæmolysis are to be found in the jaundice and in certain features of the blood changes.

Jaundice.

The term jaundice is here used as embracing all the processes concerned in the disintegration of the hæmoglobin molecule. These include the manufacture of bile pigments and the excretion of disintegration products, as well as the actual pigmentation of the skin. Such a wide use of the term is justified only by the fact that at present there is no other which adequately expresses the sum total of the processes involved.

Although the close relationship between the formation of the bile pigments and the cleavage of the hæmoglobin molecule has long been recognized, we are still ignorant of many of the details of the chemistry and mechanism of the two processes. The hypothesis of Addis is at present regarded as the most instructive. It is summarized as follows by Drinker:[18]

> Addis believes that hæmoglobin is separated by the liver cells into a pigment, hæmochromogen, and globin. By removal of the iron the pigment moiety is converted into bilirubin and excreted into the intestine, where, through reduction, urobilinogen is formed. This compound Addis believes may be re-absorbed and polymerized to urobilin and eventually again become part of the hæmoglobin molecule or it may be excreted in the fæces and urine. In both of these latter instances the action of oxygen results, soon after passage, in the formation of urobilin.

While this theory may correctly explain the normal process, it does not take cognizance of the fact, established by Whipple and Hooper,[19] that bile pigment and urobilin may be formed when the liver and spleen are excluded from the circulation. It must be admitted, therefore, that jaundice may be purely hæmatogenous and is not always hepatogenous, as was previously thought. Clinical evi-

dence in support of this view is afforded by the occurrence in certain diseases of "dissociated jaundice," that is, the presence of bile pigments in the plasma in the absence of bile salts. As McNee[20] puts it: "All modern work, in fact, strengthens the view that a true hæmolytic icterus apart from the liver does occur."

The actual site of the hæmolysis is unknown. Probably it never occurs intravascularly to any extent in health and seldom in disease, otherwise hæmoglobinuria and the acutely toxic symptoms due to hæmoglobinæmia would be more frequent. It is generally considered that hæmolysis is mainly intracellular, the large endothelial cells of the spleen, liver, marrow, lymph glands and blood vessels all sharing in the process. Evidence of its occurrence is afforded by the presence in the plasma and in the urine of certain derivatives of the hæmoglobin molecule, especially bilirubin and urobilin.

For the determination of the nature of the jaundice in any particular case it is necessary, therefore, to investigate not only the coloration of the skin, but also the distribution of pigment in the blood stream and the urine. It may be said at once that the results in the present series afford sufficient justification for regarding the jaundice as a result of excessive hæmolysis.

The pigmentation of the skin in the affected members of this family, though constantly present, was not very definite. In the milder cases it was manifested only as a sub-icteric tint of the conjunctivæ and the complexion, though sallow, could not be described as definitely jaundiced. In the more severe the conjunctivæ were definitely icteric and the colour of the skin had deepened to the muddy yellow tint often seen in pernicious anæmia, though the characteristic lemon colour of this latter disease was not observed. With the slighter degrees of pigmentation repeated observations with the use of Gmelin's and Cole's tests always demonstrated the absence of bile pigments in the urine. Spectroscopic estimations, however, invariably showed that the urinary urobilin was much above the normal figure. The depth of pigmentation varied from time to time in individual cases. During exacerbations the urine of adult patients frequently contained large quantities of bile pigment which disappeared as the jaundice lessened. But in the children the exacerbations were not accompanied by choluria.

More constant and reliable evidence of blood destruction and a rough indication of its amount are afforded by the presence and degree of bile staining of the serum. For the detection of bile pigments Gmelin's test was used. Blankenhorn[21] has described the technique of the test, which, though not very delicate, is free from fallacies. By its use the constant presence of bile pigments in the blood of every case was demonstrated. In a general way their amount, as judged by the intensity of the reaction, parallels the degree of coloration of the serum and the depth of pigmentation of the skin.

Van den Bergh's test, recently described by McNee,[20] is not only more delicate, but, in addition, gives information as to whether the jaundice is obstructive or hæmolytic. Miss Cowan, of the Walter and Eliza Hall Institute, has been good enough to apply it to the serum of two patients. Her investigation showed that two units of bilirubin were present, one being normal, and that the jaundice was of non-obstructive type. The presence of urobilin also was demonstrated spectroscopically in every serum examined. In two cases, Dr. Maxwell, University Lecturer in Physiology, confirmed this finding by means of Ehrlich's aldehyde test.

The presence of bile pigment in the serum and its absence in the urine is susceptible of two explanations. Either it is so attached to some constituent of the blood that the kidney does not eliminate it, bile pigment as such only appearing in the urine when the saturation point of the blood is exceeded, or it is broken down in the kidney cells and excreted as urobilin. The point could be settled by comparing the amounts of bile pigment and urobilin in the blood and urine, but the methods available for quantitive estimation of the former are difficult to carry out and not sufficiently accurate for this purpose. Working with cases of pernicious anæmia, Blankenhorn[21] found that, with bile salts present in the blood, urobilin was commonly absent from the plasma, though present in the urine. This would suggest that urobilin may be a product of the activity of the kidney, but the findings need confirmation before such a deduction can be widely applied. In the cases under discussion a simpler explanation is feasible, that is, that the bile is held back by the kidney unless a considerable amount is present in the blood, while the less complex molecule of urobilin is excreted in the urine. This conclusion, however, is only tentative and is open to revision in the light of further investigations on pigment metabolism.

The tests for bile salts are tedious and open to a number of objections. They were not attempted in this series, but the point as to their presence in the blood is important as indicating whether the jaundice is of the "dissociated type." It is generally agreed that the toxic symptoms of obstructive jaundice, such as pruritus, bradycardia and the hæmorrhagic tendency are due to the bile salts rather than the pigments. Such symptoms were absent in all cases of this series, even when the jaundice was severe, a fact which certainly suggests an extrahepatic source of the pigment and an absence of bile salts in the blood stream.

The main features of the jaundice in the affected members of this family may be summarized as follows: Pigmentation of the skin and mucous membranes is, as a rule, slight, but is subject to increase at irregular intervals. Bile pigments are always present in demonstrable quantity in the blood serum. Though they are generally absent from the urine, they appear in the adults during exacerbations. The jaundice, therefore, is not truly acholuric, bile pigments being absent from the urine only as long as their amount in the blood stream remains small; when larger quantities of pigment are found in the blood, choluria occurs. Excess of urobilin is always present in the urine. Bile pigments always occur in the blood serum in demonstrable quantity. Van den Bergh's test indicates

that the jaundice is of non-obstructive type. The absence of the well-known clinical symptoms of cholæmia suggests the absence of bile salts from the blood and affords additional evidence that the jaundice is extra-hepatic.

All these observations tend to support the conclusion that the jaundice is hæmatogenous. Whether the liver is concerned at all cannot be definitely determined. Formerly the explanation offered was that the large quantity of available pigment, due to the unusual hæmolysis, embarrassed the action of the liver so that bile was produced in excess of normal quantity and perhaps altered in composition. As a result the bile capillaries became blocked and absorption by the blood stream and pigmentation of the skin followed. The frequent occurrence of gall stones in patients suffering from hæmolytic splenomegaly was thought to lend support to this theory. Undoubtedly they do occur; two patients in this series have been operated on for gall stones some years after their spleens were removed. It may also be conceded that the first part of the explanation contains an element of truth, but there is no proof that actual obstruction of the small ducts occurs.

As a rule there is no clinical evidence of any pathological change in the liver. Most observers agree that cirrhosis is unusual in hæmolytic splenomegaly, though Giffin[22] found microscopical evidence of its presence in two advanced cases. These may be regarded as isolated exceptions, but it is conceivable that continued overwork might ultimately result in fibrosis. In the present series no enlargement was noted in any of the children. In only two of the adults, both with long-standing disease, the smooth, lower border could be felt two fingers' breadth below the costal margin. When splenectomy was performed, the liver was always carefully examined, but no alteration in size, appearance or consistence was noticed. It is, therefore, reasonable to conclude that any changes that occur in the liver and bile ducts are not sufficient to account for the jaundice.

Recognition of the fact that the jaundice depends mainly, if not entirely, on hæmolytic activity, not only accords with the available evidence, but also furnishes an important clue to the nature of the disease under consideration.

The Blood Picture.

The main features of the blood picture have already been described. It is advisable, however, to recapitulate briefly those changes which are dependent on excessive hæmolysis. Direct evidence of abnormal blood destruction is furnished by the presence of degenerative types of erythrocytes, such as very irregularly shaped cells, especially microcytes. Rous and Robertson[23] have shown that these are to be regarded as the products of fragmentation of erythrocytes. The constant occurrence of regenerative forms is an indirect result of excessive hæmolysis. In the attempt to replace the destroyed cells the marrow is over-stimulated and immature forms, such as polychromatophilic, nucleated and reticulated red cells, appear in the circulating blood.

It has already been remarked that the jaundice fluctuates in intensity, deepening at such times as blood destruction becomes more active. No corresponding variations in the blood picture could be made out. In Case IX., detailed above, the red cell count was higher at the time of an exacerbation of jaundice with choluria than during a remission three months later. These periods of increased hæmolytic activity were generally accompanied by intensification of the general symptoms and a rise of temperature to 38.4° C. or 38.8° C. (101° F. or 102° F.). Their occurrence could not be correlated with any obvious cause, such as infection or, as noted by some observers,[24] with exposure to cold. As the paroxysm passed off, the severity of the symptoms abated and the temperature fell to normal.

These exacerbations, aptly described by Chauffard as *"crises de déglobulinization,"* are a striking feature of all the recorded cases of hæmolytic splenomegaly. As shown by the cases described by Elliott and Kanavel,[25] they are often more intense than in the present series. The findings as regards the actual depth of jaundice also vary considerably in different families. Chauffard's statement that "the patients are more icteric than sick" cannot be applied to the members of the family under review or to several other patients whose illness is recorded in the literature. Despite these variations there is general agreement as to the nature and significance of the jaundice associated with hæmolytic splenomegaly.

Miscellaneous Clinical Features.

Particular attention was directed to the condition of the superficial lymphatic glands, but no enlargement was noted in any of the patients.

Gastric analysis of Case XXII., male, *ætatis* fourteen years. with only slight anæmia, showed absence of hydrochloric acid after Ewald's test meal.

The wedge-shaped fatty thickenings of the conjunctivæ described in the account of Case IX. also occurred in another gravely affected adult, but were not present in any of the children examined. Brill and Mandelbaum,[13] describing a similar condition in cases of Gaucher's splenomegaly, state that it occurs in no other disease and regard it as an important diagnostic point. Whatever may be the cause of this conjunctival thickening, its presence in the cases of this series indicates that it is not peculiar to Gaucher's disease.

The Problem of the Inter-Relationship of the Symptoms.

The symptoms have been discussed individually only for the sake of convenience. It is obvious that their significance must be considered in the light of their relation one to the other and to the disease as a whole. That the anæmia and the jaundice depend on excessive hæmolysis is clear. The latter, in its turn, must be in some way dependent on the increased corpuscular fragility. Much else remains obscure. What is the significance of the splenic enlargement and what is its connexion, if any, with the hæmolytic activity? What is the cause of the fragility of the red cells? What is the hereditary factor at work? The pathological findings and the results of treatment must be discussed with special

reference to these problems, for their solution is essential to an understanding of the nature of the disease.

Morbid Anatomy of the Spleen.

Eight members of this family have been subjected to splenectomy. The pathological features of two of the spleens have been described by Springthorpe.[1] Five spleens removed during the present investigation form the basis of the description of the morbid anatomy of the organ in this series.

Data concerning the weights of the spleens are incorporated in the following table:

Number.	Sex.	Age.	Weight of Spleen.
VII.	Male	48 years	640 grammes
XIX.	Female	10 years	235 grammes
XX.	Male	6 years	228 grammes
XXII.	Male	14 years	291 grammes
XXIII.	Male	13 years	298 grammes

The macroscopic appearance was essentially the same in all four cases in children. The shape of the organ was preserved, the notches in the anterior border being well marked. The consistency was firm and resilient, but not hard. Patchy opacities were scattered about the capsule and some fine transparent adhesions were present along the mesial border and about the upper pole and the upper part of the external surface. The cut surface was dark brownish-red and dripping with blood. The capsule and trabeculæ appeared to be slightly thickened and the Malphigian corpuscles were large and prominent, but not increased in number. No thrombosis of the splenic vessels was observed.

The adult spleen presented a similar appearance. The absence of gross fibrosis was the most important feature, but numerous dense adhesions were present about the upper pole and posterior border.

For purposes of microscopical examination pieces of tissue from the convexity and from the neighbourhood of the hilus were fixed in formalin and in Schaudinn's solution. Sections were stained with hæmatoxylin and eosin, hæmatoxylin and picric acid, Gauduscheau's, Van Gieson's and Wiegert's stains.

The microscopical appearances of the various children's spleens were much alike, so that a general description applicable to all of them can be given, minor differences being indicated where necessary.

There was no thickening of the capsule and no increase in size or number of trabeculæ. The pulp was intensely and uniformly engorged with blood, giving it a homogeneous appearance, the proportion of nucleated cells to erythrocytes being much smaller than in the normal spleen. The sinuses were inconspicuous, but here and there an empty one stood out boldly against the congested pulp.

Examination under higher magnification showed considerable endothelial activity throughout the pulp, the cells lining the sinuses being large, with rounded nuclei, and the reticular cells generally more noticeable than in the normal organ.

The intense engorgement rendered identification of the nucleated forms rather difficult. Of the latter lymphocytes formed the largest number. Eosinophile cells, both mononuclear and poly-morphonuclear, were numerous in all the sections, but could not be said to be abnormally frequent. Polymorpho-nuclear neutrophile and "splenic" cells were also in evidence. Here and there in the sinuses less tightly packed with blood phagocytic cells could be seen. They had large, pale, oval nuclei with a well-marked nuclear membrane and several nucleoli and appeared to be stuffed with red blood cells, so that the structure and appearance of the cytoplasm could not be accurately made out. Even allowing for the fact that the intense congestion rendered them difficult of identification, these phagocytic cells could not be said to be a particularly striking feature of the sections, nor were they especially conspicuous in smears of the pulp.

The Malphigian bodies were not increased in number. In two cases (XIX. and XX.) some were much enlarged and formed a conspicuous feature of the sections (see Figures III. and IV.). The increased size was mainly due to a central aggregation of loosely packed cells having large oval nuclei with a well-marked nuclear membrane and two or three prominent nucleoli. The cell bodies were irregular in shape, often stellate, with processes continuous with the reticulum which could be plainly discerned in intimate association with them. In the interstices between them lay a few lymphocytes, poly-morpho-nuclear neutrophile and red blood cells. Outside this central area of relatively pale appearance was a zone of tightly packed lymphocytes. Occasionally a third zone of mixed lymphocytes and cells like those in the central area was observed. Undoubtedly these large cells belong to the reticulo-endothelial structure of the spleen, which becomes prominent here and there along the arterioles. Seemingly these exaggerations of the reticulum are of spherical shape, since prolonged search revealed no Malphigian bodies with a pale centre cut longitudinally. A similar appearance to that described can be seen in some sections of normal spleen, but the central pale area is rarely as large as in these cases, nor is it as sharply demarked from the zone of lymphocytes round about it. The change, however, is one of degree rather than of kind and cannot be said to constitute an abnormal or pathological feature. Further, the spleens of the other two children (Case XXII. and Case XXIII.) showed this appearance very seldom and in much less marked fashion; indeed, the Malphigian bodies in these instances were regarded as strictly normal in structure. Thickening of the arterioles was noticeable in all four cases, the change as a rule affecting all the coats in like degree, but in one case (XXII.) endothelial activity was the predominant feature, the lumen of some of the smaller vessels being almost occluded. The arteries, too, were thickened, the main increase being in the adventitia without hypertrophy of the *media* or *intima*. Sections stained with Van Gieson's and Wiegert's stain did not show any increase in fibrous or elastic tissue except in the vessel walls.

The adult spleen (Case VII.) showed the same

apparent deficiency of nucleated cells, but the engorgement was less intense and numbers of empty sinuses were a striking feature of the sections. The endothelium of the sinuses stood out prominently, the cells being irregular in shape, with round, deep-staining nuclei and containing quantities of pigment. The deposition of the latter must, in part at least, be attributed to the fact that formalin fixation only was used for this spleen. Throughout the organ the reticulum was strongly marked, but there was no general fibrosis or increase in elastic tissue. In the sinuses numerous phagocytic cells were seen distended with pigment granules, but none was found containing red blood cells. This again may have been the result of formalin fixation. Otherwise the cell constituents of the pulp were similar to those of the younger spleens, but the increase in mononuclear and poly-morpho-nuclear eosinophile cells was more noticeable in this case. The thickening of the arteries and arterioles was perhaps the most striking feature of this spleen. All the coats seemed to be involved in the change, endothelial hypertrophy occurring constantly, whilst the increase of the adventitia of the arteries was very pronounced. The capsule was not thickened, nor was there any increase in size or number of the trabeculæ.

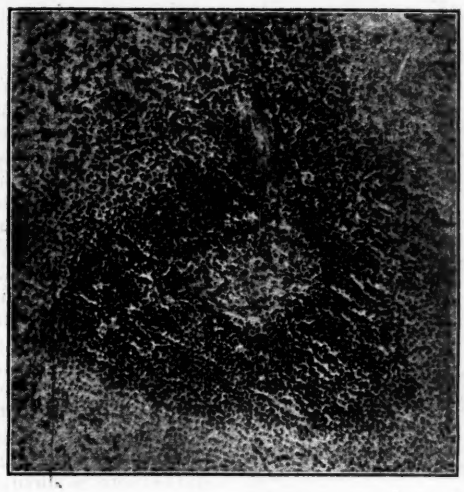

FIGURE III..
Low Power Drawing of Malphigian Body. To show hypertrophy of reticulo-endothelial cells. Leitz Oc. II., Obj. 3.

The appearances of another adult spleen from one of the earlier patients (Case XI.), which has been re-examined, are almost identical with those described here.

Throughout the series the most striking feature of the microscopical anatomy of the spleen is the intense engorgement with blood. Other constant changes are the increase of reticulo-endothelial structure and the thickening of the coats of both arteries and arterioles. Though the latter is probably a direct result of the increased blood supply, these appearances raise the question, to be answered later, as to whether there is a syphilitic factor at work. Phagocytosis cannot be said to be abnormally prominent and the increase in number of eosinophile cells is not of sufficient degree to be regarded as a constant pathological finding. There appears to be no tendency to general fibrosis or to "strangling" and disappearance of the Malphigian bodies.

Probably because of this lack of distinctive features, the morbid anatomy of the spleen in hæmolytic splenomegaly has hitherto received little attention. Krumbhaar could collect from the literature descriptions of only fifteen spleens. Practically all of them showed congestion and pigmentation, with an increase in the number of large phagocytic cells. As a result of his investigations Krumbhaar[3] says: "Pathological study has yielded little in the way of establishing a constant and characteristic pathological picture."

As a result of the present investigations a more definite statement is possible, namely, that no specific or characteristic lesions occur in the spleen in hæmolytic splenomegaly. The findings are all attributable to increased functional activity, that is, exaggeration of the normal hæmolytic function and the resulting vascular congestion. The significance of this conclusion may be illustrated by a comparison with splenic anæmia in which fibrosis of the spleen is the essential feature, indicating a local lesion which results in changes in other organs, with their concomitant symptoms. The absence of pathological lesions in the spleen in hæmolytic splenomegaly strongly suggests that the fundamental pathogenic factors must be sought elsewhere. This agrees with Banti's[26] conclusion, admirably expressed as follows: "These structural modifications represent simply the anatomical substratum of the hæmolytic processes and not that of the malady on which these processes depend."

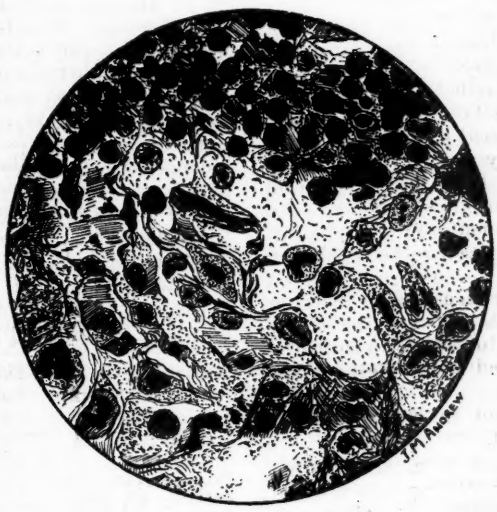

FIGURE IV..
High Power Drawing of Malphigian Body. To show hypertrophy of reticulo-endothelial cells. Leitz Oc. II., Obj. 1/12, oil immersion.

The Question of Syphilis.

Not unnaturally the possibility of a syphilitic element in the production of the long series of cases in this family has been frequently raised. The first case (VIII.) observed by Springthorpe in 1903 presented, in addition to

anæmia, jaundice and splenomegaly, chronic deep indolent ulcers of the inner aspect of the leg on both sides and the presence of a syphilitic infection was held to be very probable. Energetic treatment with iodide and mercury and sodium cacodylate failed, however, to effect permanent improvement in the general symptoms or in the ulceration. The latter, indeed, persisted until the time of the patient's death in 1921 at forty-six years of age. Similar ulcers occurred in another patient (Case VII.), but healed after some years, leaving pigmented tissue-paper scars. Two Wassermann tests with the serum of this patient were made, one giving a feeble, partial reaction and the other failing to yield a reaction; a vigorous course of anti-specific treatment with mercury and iodide and nov-arseno-benzol had no appreciable effect. It is interesting to note that intractable ulcers of the legs have occurred in several other patients recorded in the literature.[27] They are usually attributed to trauma. This somewhat inadequate explanation is the best that can be offered at present.

The appearance of endothelial activity in the spleen was also held to suggest a syphilitic origin. Reference to the description of the morbid anatomy will show that the changes there described cannot be considered typically syphilitic. The most suggestive feature, the thickening of the vascular coats, is susceptible of another explanation and the typical intimal hypertrophy, leading to obliterative endarteritis, is an infrequent finding.

Further, the well-established facts that a syndrome indistinguishable from splenic anæmia and an anæmia of pernicious type with a considerable hæmolytic element may both be caused by syphilis demand consideration in this connexion.

Finally, the evidence afforded by the results of the Wassermann test in this series must be examined. Dr. N. Hamilton Fairley, of the Walter and Eliza Hall Institute, kindly undertook the investigation of the blood of sixteen individuals, comprising ten affected and five unaffected members of the family and one collateral (husband of Case XI.). Both Harrison's and the ice-box method were used in each case. With thirteen sera no reactions were obtained; three yielded equivocal results. The latter on further investigation proved to be due to an anti-complementary activity of the serum and on allowing for this a second specimen in each instance gave no reaction. Eight specimens were also examined at different times in the University Laboratory, five not yielding reactions and three giving "partial" reactions. The latter may also have been due to anti-complementary tendency in the serum, but the point was not investigated.

In spite of some suspicious clinical features, therefore, it may be said that, taking into account the failure of anti-syphilitic treatment to effect permanent improvement, the histology of the spleen and the results of Wassermann tests, syphilis as an ætiological factor can be excluded.

Treatment and Results of Splenectomy.

The non-operative treatment of the patients in this series can be dismissed very briefly. At different periods patients have been subjected to medicinal treatment with a number of hæmatinics and, as mentioned above, anti-syphilitic measures have been used extensively in two. Whilst in hospital there has been some symptomatic benefit and improvement in the blood count. That this may occur without any drug treatment has been pointed out in connexion with Case XX., which is quoted above (see Figure II.). In no instance has medicinal treatment produced any lasting benefit.

No opportunity has arisen for the use of X-rays or radium. Applied to the spleen, these agents might be expected to diminish its functional activity and so lessen hæmolysis. They should, therefore, be of use in those patients on whom it is impossible to attempt splenectomy. A patient, belonging to another family at present under observation, has just commenced a course of applications of deep X-ray therapy to the spleen. It is hoped by this means to improve her general condition, which is very low, to such a degree that operative treatment can be undertaken. The result is being watched with interest, for I am not aware of any previous records of X-ray therapy in hæmolytic splenomegaly.

Removal of the spleen has effected striking and permanent results in this series of cases. Eight splenectomies have been performed without operative mortality. The effects of the operation will be discussed under two headings, immediate and remote.

Immediate Results of Splenectomy.

During the present investigation splenectomy has been performed on five patients—one adult and four children. Two were performed at the Melbourne Hospital by Mr. T. H. Boyd and two by Mr. H. D. Stephens and one by Mr. W. G. D. Upjohn at the Children's Hospital. The adult patient (Case VII.) presented great difficulty inasmuch as the spleen was uniformly and densely adherent to the surrounding structures. Sixteen days before the patient developed signs of a left basal pleurisy which apparently cleared up in a week. The day after the splenectomy, however, signs of a left basal pneumonia were detected and a few days later sloughing of the wound occurred. It is reasonable to suppose that these results followed the lighting up of a smouldering infection at the base of the lung by the trauma of operation.

Despite these accidents, immediate benefit was noted, as is indicated in the following blood counts:

BLOOD COUNTS OF CASE VII..

Date.	Red Blood Corpuscles.	Hæmoglobin.
December 10, 1920 ..	2,050,000	55%
January 12, 1921 ..	2,000,000	45%
February 1, 1922[1] ..	—	—
February 12, 1922 ..	3,700,000	60%
April 18, 1922	4,800,000	70%

When last seen, eighteen months after operation, this patient's improvement was maintained.

[1] Splenectomy performed

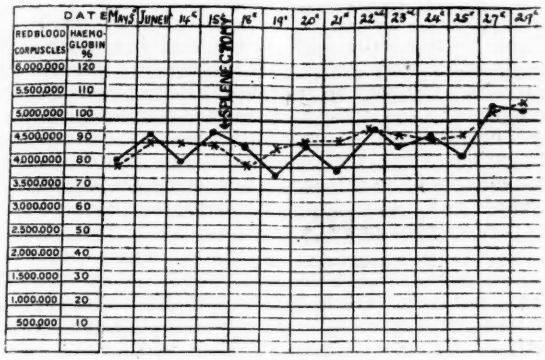

FIGURE V..
Graph Showing Blood Changes in Case XIX.. Post-operative improvement in anæmia.
Unbroken line = Red blood corpuscles per cubic millimetre.
Broken line with crosses = Hæmoglobin percentage.

In all four children fine membranous adhesions were encountered about the upper pole and inner surface, but they did not interfere with the mobility of the organ, which was removed without difficulty. Nevertheless one patient (Case XXIII.) developed a left basal pleurisy with effusion eight days later, which subsided after aspiration and retarded his recovery only very slightly. The other three had fever up to 38.3° C. (101° F.) for four to six days after operation, but no sign of trouble could be detected at the left base and the blood examinations showed no evidence of an exacerbation of hæmolysis or other disturbance.

The effect of splenectomy on the anæmia is shown in the accompanying graphs of Case XIX. (see Figure V.). The patient (Case XXIII.), despite his pulmonary complications showed even greater improvement (see Figure VI.). The early results as regard the anæmia were equally good in the two remaining patients, one of which (Case XX.) has been illustrated in Figure II..

The effect of splenectomy on the white cells was less constant. In all three uncomplicated cases the patients showed a well-marked post-operative

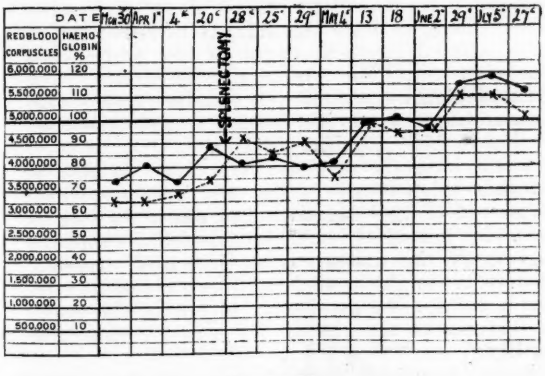

FIGURE VI..
Graph Showing Blood Changes in Case XXIII.. Post-operative improvement in anæmia.
Unbroken line = Red blood corpuscles per cubic millimetre.
Broken line with crosses = Hæmoglobin percentage.

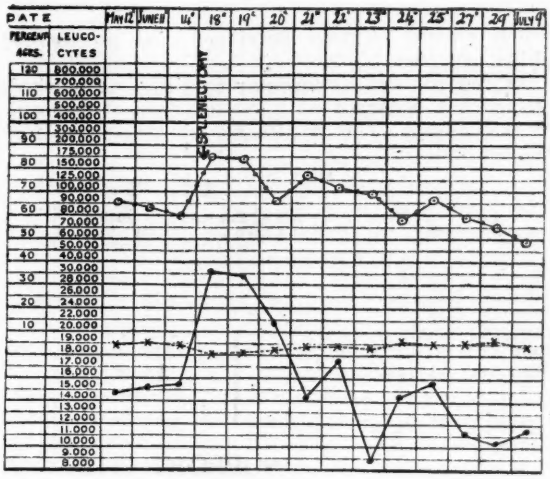

FIGURE VII..
Graph Showing White Counts in Case XIX.. Post-operative leucocytosis; no eosinophilia.
Unbroken line = Total white count.
Unbroken line with rings = Percentage of poly-morpho-nuclear cells. Broken line with crosses = Percentage of eosinophile cells.

leucocytosis; in one a definite and persistent increase of eosinophile poly-morpho-nuclear cells occurred, while the other two showed no change in the percentage of these cells. The number of poly-morpho-nuclear mast cells showed no change as a result of operation. These results are illustrated by the graphs of Cases XIX. and XX. (see Figures VII. and VIII.).

As might be expected, the post-operative leucocytosis was greatly prolonged in the patient in

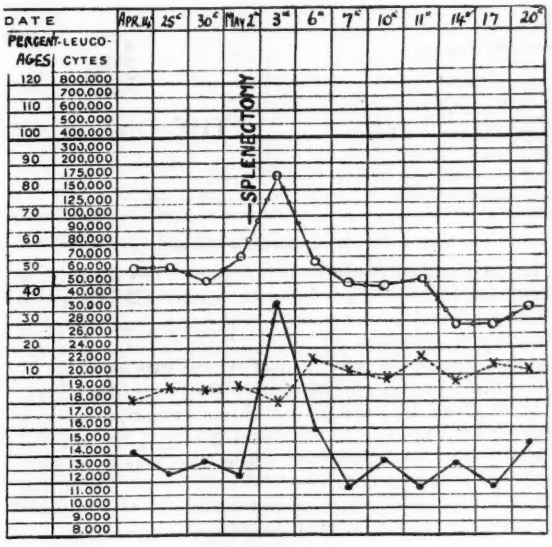

FIGURE VIII..
Graph Showing White Counts in Case XX.. Post-operative leucocytosis; marked eosinophilia.
Unbroken line = Total white count.
Unbroken line with rings = Percentage of poly-morpho-nuclear cells. Broken line with crosses = Percentage of eosinophile cells.

whom pleural effusion developed, but no eosinophilia occurred.

As regards the corpuscular fragility, no marked change has occurred as a consequence of removal of the spleen. The results are shown in the following tables:

CASE XIX..

Date.	Percentage Dilution of Saline Solution at which Hæmolysis Commenced.
June 10, 1921	0.475
June 16, 1921	0.475
June 17, 1921[1]	—
June 29, 1921	0.500
September 30, 1921 ..	0.475

CASE XX..

Date.	Percentage Dilution of Saline Solution at which Hæmolysis Commenced.
July 21, 1921	0.525
May 2, 1921[1]	—
May 20, 1921	0.525

CASE XXII..

Date.	Percentage Dilution of Saline Solution at which Hæmolysis Commenced.
May 24, 1921	0.525
July 7, 1921	0.525
July 12, 1921[1]	—
July 28, 1921	0.525

CASE XXIII..

Date.	Percentage Dilution of Saline Solution at which Hæmolysis Commenced.
April 21, 1921	0.525
April 21, 1921[1]	—
May 11, 1921	0.600
May 30, 1921	0.600
July 27, 1921	0.525
August 27, 1921	0.525

In two cases, therefore, no immediate alteration occurred, but in two others an increase in fragility followed, but the pre-operative figures was restored after three months.

Splenectomy at once caused the disappearance of the pigmentation of the skin. Further, bile disappeared from the serum of three patients, as evidenced by the results of Gmelin's test, on several occasions after operation, while the excess of urobilin in the urine completely disappeared. Van den Bergh's test was done on the serum of the patient (Case VII.) eighteen months after splenectomy. It gave a faint indirect reaction, the quantity of bile pigment present being within normal limits. The jaundice, therefore, was completely abolished by removal of the spleen.

[1] Splenectomy performed.

Even these results and figures, striking as they are, do not convey adequately the general improvement which followed splenectomy. Before operation the patients were dull and listless; afterwards they were bright, active, apparently normal children. The patient, Case XX., was practically bed-ridden; three months after splenectomy he commenced going to school and was making rapid progress when last seen five months later.

Remote Results of Splenectomy.

Two patients (Cases VIII. and XI.) observed eighteen years after splenectomy exemplify the late results. Dr. Springthorpe's first patient (Case VII.) was desperately ill before operation[(1)] and had been in and out of hospital for the previous thirteen years. Her health was greatly improved after splenectomy, but the ulceration of the legs, which has already been alluded to, did not clear up. Throughout the remainder of her life she lived in the direst poverty and bore four children, but survived for eighteen years, eventually succumbing to broncho-pneumonia. Examination on May 12, 1921, revealed that the blood contained 3,570,000 red blood corpuscles per cubic millimetre, that the hæmoglobin value was 68% and that there were 18,700 white blood cells to the cubic millimetre. The film showed an occasional misshapen and a few polychromasic red cells. Two normoblasts were noted among three hundred white cells. The differential count of the leucocytes showed no abnormal features. There was no reaction of the serum to Gmelin's test. The corpuscular fragility was indicated by the commencement of hæmolysis with 0.500% of saline solution. It is difficult to know how much of the anæmia to attribute to factors other than the familial disease, but it is interesting to note the persistence of increased corpuscular fragility.

Dr. Springthorpe's second patient (Case XI.) was less ill before operation and afterwards lived in somewhat happier, though very poor, circumstances.[(1)] She has had seven children, of whom five survive. The result of examination almost exactly seventeen years after removal of the spleen was as follows: Red blood corpuscles, 4,600,000; hæmoglobin value, 70%; white blood corpuscles, 16,000. There were no abnormal cells, either red or white. The differential count of the white cells revealed a condition within normal limits. The serum yielded no reaction to Gmelin's test. Corpuscular fragility was increased, the hæmolysis commencing in 0.500% saline solution.

Summarizing the results of treatment, it may be said that splenectomy is the only measure which has proved of real benefit. The operative risk is negligible; immediate improvement follows and the progress of the disease is permanently arrested. Splenectomy might be said to effect a complete cure were it not for the persistence of one of the essential features of the disease—increased corpuscular fragility.

Similar beneficial results in hæmolytic splenomegaly have been recorded by other observers. Spencer Wells in 1888 reported the first patient operated on for this condition. Twenty-six years later, that is, in 1914, Lord Dawson[(28)] reported that the

patient was alive and well, but the red cells still showed increased fragility. Of forty-eight patients whose histories were collected from the literature by Elliott and Kanavel[25] in 1915, forty-six are reported as cured. Only two died, one shortly after operation and one six weeks after, from sepsis. At the Mayo Clinic[29] up to 1920 thirty-two splenectomies had been performed with one hospital death. One patient was living over nine years after operation. Only very rarely, in fact, have unfavourable results been recorded and the small percentage of deaths is almost entirely due to complications. The corpuscular fragility generally persists, despite the symptomatic improvement. Sometimes, however, the resistance returns to normal shortly after operation, as instanced by the patients of Bland Sutton and Wynter,[30] Moynihan[31] and others. The variations in this respect must be taken into account in considering the pathogenesis.

The frequent persistence of the increased fragility, like the pathological findings, indicates that the *causa causorum* cannot be located in the spleen. Nevertheless, the effect of splenectomy on the symptoms is so striking and so permanent that the indication for operation is clear. It should be performed as early as possible in all cases where the disease is causing any disability. To delay until the spleen is large and adherent and the general condition poor is to court the occurrence of post-operative complications. Expectant treatment is justifiable only in those rare cases in which symptoms are so slight as to permit the patients to lead a normal, active existence. In the great majority of patients early splenectomy is therefore indicated.

Diagnosis.

It has been shown that the affected members of this family present a constant and characteristic clinical picture. The minor differences found in individual patients are attributable to variations in the severity of the disease. The salient features, common to all the cases, are splenomegaly, increased corpuscular fragility, evidence of excessive hæmolysis, especially jaundice of hæmatogenous origin, anæmia, absence of specific pathological changes in the spleen and lasting benefit from splenectomy. These characteristics bring the cases under review into line with those recorded by other observers as examples of hæmolytic splenomegaly or acholuric jaundice.

As long ago as 1885 Murchison[32] described an instance of chronic jaundice affecting several members of a family, but he made no mention of splenic enlargement. It is interesting to note that Hutchison and Panton,[33] on re-investigating this family in 1909, found that the disease affecting its members was hæmolytic splenomegaly. Though several similar cases were published during the succeeding years, it was Hayem's[34] description of the acquired type in 1898 that established acholuric jaundice as a clinical entity. The existence of a similar condition in a familial form was recognized by Minkowski[35] in 1900. The most important subsequent contribution was that of Chauffard,[17] who in 1907 demonstrated increased corpuscular fragility in both forms of the disease.

The number of cases, both acquired and familial, recorded in the literature is now considerable. There is general agreement as to the constancy of the main symptoms. Minor differences are, however, found in various cases, especially as regards the size of the spleen and the depth of jaundice. In consequence, various designations have arisen. In particular, Banti[26] has set up a distinction between two conditions obviously closely allied, which he calls "hæmolytic splenomegaly" and "hæmolytic jaundice." His arguments are not convincing and it seems best to recognize that until an ætiological classification is possible, we must regard the term acholuric jaundice as descriptive of a group of diseases which may eventually be accurately subdivided. The multiplication of sub-varieties, each with a cumbersome name, only leads to greater confusion and renders future investigations more difficult. For the present a name which denotes the whole group, should be used for all cases falling within its confines. Banti refers to it as the "splenohæmolytic family." "Acholuric jaundice" is the term most commonly used, but it has already been shown to be incorrect. "Hæmolytic splenomegaly" appears preferable, as being more succinct and best indicating the fundamental features of the condition. Adding the necessary qualification, I have therefore used the term "familial hæmolytic splenomegaly" to describe the cases under review.

Differential Diagnosis.

The differentiation of hæmolytic splenomegaly from other members of the idiopathic splenomegaly group has already been sketched. It is here necessary only to repeat that its special distinguishing features are the increased corpuscular fragility and the abnormal hæmolysis.

Outside this group, pernicious anæmia is the only disease which requires consideration in the differential diagnosis. The fact, emphasized by Hunter,[36] that many of its symptoms are dependent on hæmolysis brings it into close relationship with hæmolytic splenomegaly. The occasional similarity of the blood picture in the two conditions has already been referred to. Blankenhorn[21] has shown that the characteristic pigmentation in pernicious anæmia is due to a hæmatogenous jaundice, identical with that observed in the present series.

There are, however, essential differences between the two diseases. In pernicious anæmia the corpuscular fragility is normal or decreased and a myelotoxic factor, an agency directly poisoning the bone marrow, is at work. The blood changes are, therefore, more intense and the progress of the disease more relentless. The spleen is only slightly enlarged and no familial incidence is found. Splenectomy can, at best, only be described as palliative.

Though the clinical distinction between them is clear, the two conditions are, as it were, linked together by their common hæmolytic factor. This relationship lends greater point to the discussion of the pathogenesis of hæmolytic splenomegaly, itself a rare disease, inasmuch as a little light may be thrown on the problem of the nature of pernicious anæmia.

The Nature of the Disease.

The fundamental factor in the pathogenesis of this disease appears to be the persistent excessive hæmolysis. This statement indicates as questions of prime importance: What is the cause of the hæmolysis? Where does it occur? What is its relation to the increased corpuscular fragility? By what means does splenectomy put a stop to it? Certain aspects of these questions have already been touched on and further discussion of the nature of hæmolysis is beyond the scope of a paper mainly concerned with clinical observations. So, too, the functions of the spleen, which remain obscure, in spite of Pearce's brilliant work, can be considered only in so far as they throw light on the practical aspect of the matter. Attention will, therefore, be directed mainly to the question as to how and why splenectomy alleviates the symptoms. The answer to this would not only elucidate the nature of this particular disease, but would clarify our conceptions of the whole group of hæmolytic anæmias, including pernicious anæmia.

The pathogenesis of hæmolytic splenomegaly has long been a matter of lively debate. Two divergent schools of thought claim the support of various French and Italian authorities. The one, with Widal as its protagonist, holds the view that the primary lesion is in the blood, a dyscrasia of the red cells. The other, originated by Minkowski and supported by Chauffard, would incriminate the spleen as the cause, direct or indirect, of the exaggerated hæmolysis. There are certain difficulties in the way of complete acceptance of either view.

If the essential lesion is the fragility of the red cells, why has splenectomy such a striking effect though the fragility often remains? After experimental removal of the spleen in dogs, hypertrophy of the endothelial cells of the lymph glands and liver occurs and these cells are actively phagocytic towards erythrocytes and their disintegration products. There is evidence that a similar process occurs in man. It might therefore be expected that destruction of the fragile corpuscles would take place in other organs after removal of the spleen and soon reach its previous level. If this were so, the symptoms dependent on hæmolysis, such as anæmia and jaundice, though relieved at first, would soon recur. This is not in accord with the facts. Though the fragility of the red cells must undoubtedly facilitate their destruction, some additional factor must cooperate in actually bringing it about. The actual nature of the change in the erythrocytes remains obscure. Ward[27] suggests that it may be physical and molecular. Possibly it is due to the chemical action of a toxic substance, for a strictly comparable effect is produced by certain poisons, notably toluylendiamine. The latter is the simpler and more tangible conception.

On the other hand, if the spleen is the actual cause of the abnormal hæmolytic activity and not merely its main site, why does splenectomy not restore the normal resistance of the red cells? That it does so sometimes is definitely established and in these cases one might regard the red cells as being "fragilized" by some product of splenic activity. This explanation does not apply to the cases under review, since the fragility remains after operation. The absence of specific lesions in the spleen, though it does not necessarily imply the absence of functional derangement, suggests that the cause of the disease must be sought elsewhere.

Neither theory is of itself wholly satisfactory. While the corpuscular dyscrasia is an essential feature in the ætiology of hæmolytic splenomegaly, some other factor must also be at work. It may be that the spleen elaborates some substance which promotes the destruction of the fragile corpuscles. This substance might, for example, be of the nature of an amboceptor or an opsonin, facilitating the action of an unidentified hæmolytic poison or of the phagocytic cells of the spleen itself and other organs. Splenectomy, by putting a permanent stop to the production of this intermediary body, retards the hæmolytic process. This conception may be made clearer by a comparison with the effect of splenectomy in pernicious anæmia. Here the production of symptoms seems to depend on the action of a hæmolytic poison sufficiently virulent to destroy normally resistant corpuscles without the aid of any intermediary substance of splenic origin. Removal of the spleen has, therefore, a mechanical effect only and as soon as hypertrophy of the phagocytic cells of other organs occurs, hæmolysis again becomes excessive and the symptoms recur.

I venture to suggest, therefore, that both the corpuscular dyscrasia and the specific activity of the spleen are essential factors in the pathogenesis of hæmolytic splenomegaly. Both may be due to the action of a toxic substance as yet unidentified. Splenectomy permanently relieves the symptoms by abolishing the splenic factor, without which excessive hæmolysis is not possible.

The familial and acquired forms are closely related. Their inter-dependence is exemplified by another family, at present under observation, in which the disease was acquired by one of seven children of healthy parents. This patient had two children, both of whom were affected. No other case has occurred in the family. The transmitted factor appears to be a toxin which causes an inborn error of metabolism manifested by corpuscular fragility and splenic activity. Hæmolytic splenomegaly must have been introduced into the family with which this paper deals by the occurrence at some time of an acquired case among its members. The earliest generation about which records exist, shows two members probably affected, so the disease must have arisen at least as far back as their parents. The children in the present series represent, therefore, at least the fourth affected generation.

The familial factor is undoubtedly truly hereditary and the term congenital, which is often applied to these cases, is a misnomer. The disease is inborn; it does not merely appear at or soon after birth. The age of onset of symptoms is dependent on the balance between blood destruction and blood regeneration. The age at which the former gains the upper hand and so leads to the appearance of symptoms, varies in different cases. This explains the variations in the time of onset of the disease in the cases under review.

The laws governing the transmission have not been definitely ascertained. Reference to the family history (see Figure I.), however, shows certain interesting points. Direct transmission from parent to child appears to be the rule. In no case has a healthy parent given birth to an affected child. On the contrary, diseased parents often have healthy children, for example, Cases XVI. and XXI.. About half the children in each affected branch of the family are diseased. Campbell,[37] who has recently discussed this aspect of the question, says that it is difficult to fit the condition in with the Mendelian theory. Meulengracht,[38] on the other hand, considers that the disease is transmitted as the dominating characteristic in the manner of true hereditary diseases. But it seems to me that the present state of our knowledge does not justify a definite statement.

While admitting that the explanation here offered of the pathogenesis of hæmolytic splenomegaly is largely speculative, I submit that it affords a reasonable explanation of the remarkably successful results of splenectomy.

Conclusion.

In conclusion, I wish to thank those Honorary Medical Officers of the Melbourne and Children's Hospitals who have permitted me to investigate the cases of patients under their care. Much of the practical work was done in the Laboratory of the Children's Hospital. The Director and staff of the Walter and Eliza Hall Institute have given me much help and encouragement. Mr. Harold Dew's beautiful microscopical preparations of the spleens were invaluable. The work has been rendered especially pleasant by the generous cooperation of everybody with whom it has brought me into contact.

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THE PREVENTION OF DIPHTHERIA.

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FROM January, 1921, to May, 1922, inclusive there were admitted to the Narrandera Public Hospital two hundred and twenty-four patients suffering from diphtheria. Of these, one hundred and forty-two were below the age of fifteen years.

An endeavour was then made to check this disease. Swabbings were taken of all school children in the municipality and at Gillenbah. At first cultures were taken, but, owing to the unreliability of the electric current and thereby of the incubator, it was decided to rely on direct smears. These were taken, stained with Löffler's solution of methylene blue and examined carefully. In doubtful cases a second smear was taken.

In all, six hundred and sixty-three swabbings were examined and of these twenty-eight were found to be positive, *i.e.*, about 4.4%.

Of these twenty-eight carriers, twenty-five were admitted to hospital. They were given three doses of toxin-antitoxin, 0.18, 0.3 and 0.48 cubic centimetres at five-day intervals. They were not discharged until no bacilli were detected in three consecutive swabbings. The average stay of these carriers in hospital was twenty-one days. Only the long granular stained Klebs-Löffler bacillus was accepted as positive. These swabbings were taken from May 20 to the end of June.

The average monthly admissions of diphtheria

from January, 1921, to May, 1922, was 13.2. During June, July and August of this year it has dropped to seven. The average monthly admission of patients below the age of fifteen was 8.4 prior to the taking of swabbings; after that it was three.

Of the twenty-one admitted since the taking of swabbings, only nine have been children and of the total number ten have been from without the municipality. Although it is too early to make any reliable deductions, yet the results appear to have to some extent justified the amount of labour expended. In future I should recommend the Schick test, followed by toxin-antitoxin immunization.

Taking children in the municipal area, the drop was from 7.5 to 4.6 per month. During the first thirteen days of September, 1922, there have been no school children admitted.

Since writing the above report there has been a marked diminution in the number of cases of diphtheria from the municipality, although we are still getting admissions from the surrounding districts.

Since August 18, 1922, no school child from the municipality has had diphtheria as far as I know.

Reviews.

VERSION.

"THIS book is dedicated to the 'woman in travail' in the reverent hope that her 'hour' may be shortened, her 'anguish' lessened and her 'joy' made complete." This eloquent dedication embodies the main thesis of Dr. T. W. Potter's book,[1] which shortly is that it is "justifiable to perform a podalic version for the purpose of eliminating the second stage of labour and relieving the woman of the pains and agonies of child-birth, since such a proceduce in my hands has been attended with no increase of fœtal mortality and has had a lessened maternal mortality and future morbidity."

We are quite convinced that in Dr. Potter's hands version does all that he claims for it in the above paragraph, but we are equally satisfied that, if adopted as a routine measure, child-birth will be more dangerous for mother and child.

Dr. Potter also leaves out of account the fact that with his method the woman will still suffer the severe pains of the first stage, for he very properly teaches that version must never be attempted with an undilated cervix. If Australian obstetricians would refrain from the use of forceps under the same conditions, mortality, morbidity and serious injury would be lessened.

The first chapter deals with the early history of version and contains much which is interesting and instructive. Version was known to the Greeks and podalic version was described by Soranus in the second century. Until the discovery of the forceps no other procedure was available for the delivery of a living child in cases of serious malpresentation. Towards the end of the eighteenth century the forceps had gradually come into common use and less was heard of version. The old writers appear to have been wise and tactful in dealing with human nature, thus Baudelocque urges that "the operator should always proceed coolly and appear tranquil, even in the most desperate cases." Osler says much the same in "Æquanimitas."

The next chapter shows how version again came to be considered in difficult obstetrics, largely owing to the able advocacy of Sir James Simpson, Barnes and Braxton-Hicks; the latter, by introducing combined external and internal manipulations in effecting podalic version, made an epoch in the history of obstetrics. Simpson created a great impression by proving that women who in previous labours had required craniotomy, could be safely delivered of living children by version. He showed how in contracted pelvis version "caused the head to come through the imperfect brim in the most advantageous form and direction, flattening laterally under the traction."

Notwithstanding that these advocates of version were recognized to be the leading obstetricians of their time, the consensus of opinion in the medical world remained more or less opposed to version as being "more difficult and dangerous than forceps" (Cameron, "Version"; Hirst's "System of Obstetrics," 1889).

In Chapter III., "The Present-Day Employment of Version," most of the leading obstetricians in England and America are quoted and from their statements the deduction is drawn that "the present trend of obstetric practice undoubtedly seems away from rather than toward a more general employment of version as a routine procedure."

Chapter IV., entitled "The Author's Technique of Version," is the most important in the book and should be read by every practising obstetrician. It shows how the author gradually extended the sphere of employment of version and developed a technique differing materially from that described by any other writer. Every step of this technique is beautifully illustrated by photographs. The opposition to the Potter method will not be to the technique, but to the use of version for the purpose of abolishing the second stage of labour. Apart from the version itself, the author practises two procedures which must be criticized, *viz.*, "removing the placenta manually if it does not come away spontaneously in twenty minutes" and "administering pituitary directly the child is delivered." The latter procedure tends to cause contraction of the cervix and thereby to imprison the placenta. Interference with the processes of Nature in the third stage is condemned by every authority.

The last two chapters are on "Criticisms and Answers" and "Indications and Advantages." Answering the criticism that, if carried out as a routine measure by the average practitioner it would greatly increase the risks of child-birth, Dr. Potter says: "No operation should be made light of and special training is required before any man can safely perform one." This, of course, is true enough; it is also true that the forceps is frequently improperly applied. The question is: "Can version be more easily taught than the use of the forceps as Dr. Potter contends?" However, any effort to lessen the suffering of parturient women and thereby to encourage the production of more healthy and mentally well endowed babies should not be condemned without a trial. No obstetrician can read this book without interest and profit.

[1] "The Place of Version in Obstetrics," by Irving W. Potter, M.D., F.A.C.S.; 1922. St. Louis: C. V. Mosby Company; Crown 4to., pp. 138, with 42 illustrations. Price: $5.00.

ORGANO-THERAPY.

DR. GEIKIE COBB'S "Aids to Organotherapy"[1] is intended as a summary of the present knowledge of the glands of internal secretion, their development and structure, the effects of increased and decreased secretion and the methods by which their employment in treatment may be successful. The empirical use of glandular extracts is defended on the grounds that many drugs are used empirically in medicine and that without empiricism there will be no advance made.

The chapters on development and structure and on the effects of partial or complete extirpation are on sound lines, being taken to a large extent from standard works on the subject. The well-known examples of glandular deficiencies, myxœdema, cretinism and Addison's disease are dealt with in the usual way, the treatment suggested containing nothing original nor new. Small doses of thyreoid extract, such as 0.006 to 0.03 gramme (one-tenth to one-half grain) are advocated for whatever purpose the extract is administered. The effects of injections of adrenalin and of pituitary extracts and the pathological conditions in which they are usually employed, are enumerated.

When the beaten track is left, empiricism runs riot and though the author always states a case, some of his conclusions appear to be based on insufficient premisses. The language is simple and the book easy to read considering the tablet form in which its contents are administered. It may be useful to those who have not the time to study larger works.

[1] "Aids to Organotherapy," by Ivo Geikie Cobb, M.D., M.R.C.S.; 1922. London: Baillière, Tindall & Cox; Fscp. 8vo., pp. 182. Price: 5s. net.

The Medical Journal of Australia

SATURDAY, NOVEMBER 11, 1922.

Current Medical Literature.

The medical profession in Australia labours under a serious disadvantage in regard to library facilities. The earnest research student needs a first-class reference library in order that he may have ready access to all the current periodicals and the more important books. It is impossible to carry out original investigations in a satisfactory manner without such a library, for progress in medical science depends on the carrying on of research from point to point by many workers. The man who ignores the literature on the subject of his investigations, will waste his time by travelling over the same ground that others have traversed, often to find a blind end and the necessity of retracing his steps. Unfortunately the immense distance from the ancient seats of learning in Europe, the smallness of our population and the farness of one capital city from another contribute to our present position. In the larger cities there are several libraries with medical journals and books. Some overlapping takes place in certain instances, while everywhere the medical reader seeks in vain for the majority of publications needed for any one inquiry. Several attempts have been made to remedy this state of affairs. Both in Sydney and in Melbourne lists of medical journals taken at the leading libraries have been compiled and arrangements have been suggested for preventing waste through overlapping. These endeavours are admirable as far as they go, but the real solution of the problem cannot be attained in this manner.

The exchange list of The Medical Journal of Australia comprises approximately one hundred and twenty valuable periodicals, in addition to numerous publications issued by recognized public and quasi-public institutions, such as the health departments of countries in Europe and America, the Medical Research Council, the leading research institutes and the International Health Board of the Rockefeller Foundation. The journals and magazines, however, represent but a tithe of the world's medical periodicals. Little by little the list is being extended; in time, perhaps, no important journal will be missing. But the distribution of these journals after they have been studied and dealt with editorially, is based on a system of decentralization. By arrangement in 1914 it was decided that these journals should ultimately be divided between the libraries of the New South Wales and the Victorian Branches of the British Medical Association, since each of these Branches gave up its own journal in that year, together with the corresponding exchange journals. As a result, neither of these two libraries are complete as reference libraries. The libraries of the universities are but indifferently endowed for the purpose of subscribing to medical journals. At all events, the university libraries do not supplement the Branch libraries to an adequate extent. In Adelaide a wise arrangement has been adopted whereby the University and the South Australian Branch of the British Medical Association combine their efforts and ear-marked funds for a single medical library which is housed in the new Darling Building. In Sydney the Royal Society of New South Wales and the Linnean Society of New South Wales have their scientific libraries with some medical periodicals and books, but hitherto these provisions have been of small assistance to the research student in medicine. In Melbourne and elsewhere similar restricted facilities are provided.

The fact must be faced that no institution in Australia is at present prepared to expend a sufficiently large sum of money annually for this purpose. It therefore becomes necessary to attack the problem in two ways. In the first place, in each city an attempt should be made to induce the owners of libraries to centralize all medical publications. By pooling the money now spent independently by several bodies, a very valuable nucleus could be obtained. It would be disadvantageous to permit these journals and books to be distributed among several libraries, for a student seeking the literature on a particular subject would be com-

pelled to travel hours from library to library on his errand. Waste of time is intolerable.

The second expedient demands an active organizer and a spirit of cooperation between medical practitioners who now invest sums of money in current medical literature. If a number of these practitioners would join together and place their annual expenditure in a common fund, it would be possible to subscribe to those journals which are at present unobtainable in each city. The subscribers would pass these journals from one to another and, in the end, would send them to the central medical library, where they could be bound and kept for reference. In practice it would be found that the journals selected by medical practitioners would be of the more popular kind, such as are to be found in the libraries to-day. The libraries could readjust their subscriptions, so that the less popular journals are taken. In this way the one medical library in each capital city could have on its shelves complete sets of practically every medical journal in the world. Some of the copies might be several months late in arriving, but, since it appears to be choice between something and nothing, the delay would be a relatively small price to pay for a well-equipped reference library. Special mention should be made of the very meagre supply of French, Italian and German journals at present available in the Commonwealth. It is eminently unsatisfactory for the research worker to rely on abstracts published in other journals, although these abstracts are of considerable didactic value for ordinary purposes. To neglect this part of medical literature is to starve scientists in search of knowledge. A good library is an essential to every serious student. We have many beginnings, but not a single medical reference library worthy of the name.

THE PHYSIOLOGY OF THE SUPRA-RENAL GLANDS.

IN the year 1856 Thomas Addison published his now famous study, "On the Constitutional and Local Effects of Disease of the Supra-Renal Capsule." His accurate observations led to the recognition of an affection characterized by bronzing of the skin, definite asthenia, gastric and intestinal disturbances and cardiac weakness, produced by disease processes situated in the supra-renal glands. Addison died in 1860. A quarter of a century later the text-books on physiology delivered the curious lesson that, notwithstanding the clinical manifestations in persons suffering from Addison's disease, nothing was known concerning the function of these capsules fitting closely to the upper pole of the kidneys. In 1899 S. I. Golyakowski described some experiments that he had conducted on dogs with the view to elucidate the rôle of the supra-renal glands in the human economy. He sought to eliminate the greater part of these bodies and adopted ligature of some of the supplying vessels. It is uncertain to what extent he succeeded in inducing histological changes in the glands. He noted that ligation of the vessels was followed as a rule by an increase in the amount of carbonic acid utilized and of heat production. Several years later various workers endeavoured to ascertain the nature of the interrelationship between the supra-renal and the other glands of internal secretion. The discovery of the vaso-constricting action of extracts of the glands and the fact that complete removal of both glands leads to death with signs of acute disturbance of metabolism within a few days did not provide a key to the situation. Little by little it became apparent that this gland was endowed with the task of controlling within certain ill-defined limits the metabolism of food and the production of heat within the body. One of the greatest difficulties obstructing progress lay in the fact that mechanical removal of portion of the adrenal tissue yielded irregular effects, while ligature of the supplying or draining vessels left the medulla practically unaltered, although the cortex became necrotic. In certain conditions, notably those of poisoning by the heavy metals, hæmorrhages into the substance of the supra-renal glands obviously contributed to an early demise. Unfortunately the lesions were not limited to the glands and it was therefore impossible to ascribe special signs or symptoms to a loss of their normal physiological functions.

Dr. W. J. M. Scott has conducted some interesting experiments which tend to throw light on this intricate subject. In 1921 Marine and Baumann recorded an increase of heat production in many rabbits after the removal of portion of the supra-renal glands or after injury to these glands by freezing. Dr. Scott recognized that rabbits were unsuitable for these observations, partly because their heat regulation is unstable and partly because supernumerary supra-renal glands are common. He therefore carried out a series of planned experiments on cats.[1] Partial excision proved unsuitable, in that it was impossible to control the degree of functional disturbance induced, short of fatal suppression of the functions. Ligature of the veins was found to yield better results, although inconstancy of results arose as a consequence of the establishment of collateral circulation. The extent of this compensation could not be foretold nor regulated. Freezing, on the other hand, was a method by means of which the degree of injury could be varied at will. It is unnecessary to describe in detail the technique of the experiments. Care was taken to keep the cats under observation for a con-

[1] *The Journal of Experimental Medicine*, August, 1922.

siderable time before the operation and to accustom them to the restraint involved in the determination of the basal metabolism. When the injury was relatively slight, no distinct changes were noted. In especial the heat production was not increased beyond 10%. The cats ate and slept well and behaved like normal cats. When the injury was greater, the heat production was increased by more than 10% above the highest pre-operative figure. The highest reading was 44% above the highest pre-operative figure. This increased metabolism was associated with improved nutrition. The hair became sleek and shiny; the appetite was enhanced. Loss of weight was frequently observed, but in some cats there was an increase. The animals became extraordinarily alert and active and at times restless. The respiration was increased in rate and depth. Diarrhœa was common. After a time the heat production suffered a diminution. Dr. Scott is inclined to regard this as an indication of exhaustion of the thyreoid glands. The exhibition of potassium iodide led to a prompt return to normal conditions. When the injury to the supra-renal glands was so severe that death supervened sooner or later, the heat production was diminished. In extreme instances the result was indistinguishable from that of removal of both glands. After death the cortex was found to be extensively necrosed, although the chromophilic properties of the medullary cells were well maintained. It is necessary to mention that no effect was produced in cats subjected to the same operative procedure with the exception that the neighbouring tissue was frozen, but not the supra-renal glands.

The signs and symptoms in the severer forms of supra-renal insufficiency are of great interest. Gastric ulcer was seen more than once. Diarrhœa was common and usually occurred during the period of maximum disturbance. All the animals revealed an intense asthenia, with an obvious breakdown of some part of the nerve-muscle motor mechanism. In other words, the cardinal symptoms of Graves's disease were simulated in the cats whose supra-renal glands had suffered severe injury. That the failure of these glands stimulates an immediate hyperplasia of the thyreoid glands with a tendency to rapid exhaustion is demonstrated in many of the protocols. It is not improbable that the asthenia, gastric disturbance and cardiac weakness of Addison's disease depend on the primary failure of the supra-renal cortex and the later exhaustion of the vicarious thyreoid function.

HÆMOLYSIS AND JAUNDICE.

THE mechanism at work in the liberation of bile pigments to the tissues in certain forms of jaundice can only be ascertained by indirect means. Certain fundamental facts have long been recognized. In the first place it is evident that bile pigments are derived from hæmoglobin. Hæmoglobin is dissociated with the production of protein-free and iron-free pigments. The latter represent the precursors of the bile pigments. Naunyn taught that the Kupffer cells of the liver have the function of manufacturing bile pigments within the liver. The evidence in favour of this hypothesis is faulty and certain phenomena have been observed which suggest that it is untenable.

Dr. A. Bieling and Dr. S. Isaac have put forward work which must strengthen the objection to Naunyn's views and give credence to a doctrine of an initial hæmolysis in which the spleen and reticulo-epithelium play an important part in the process.[1] Observations on mice and guinea-pigs have demonstrated that if a hæmolytic amboceptor be injected into one of these animals, the red blood corpuscles take up this body and leave the circulation to accumulate in the spleen. A similar wandering of damaged red blood corpuscles takes place when a blood poison, such as phenyl hydrazin, is injected. The spleen appears to take on the qualities of erectile tissue and swells to an enormous size. The stimulation by the amboceptor calls forth the production of fresh complement and the damaged cells undergo hæmolysis. This function of the spleen to accumulate damaged red cells and to dissolve the hæmoglobin seems to be facultative. The reticulo-epithelium is capable of assuming this function vicariously. If the greater part of the reticulo-epithelium is put out of court, as can be effected by the injection of iron granules, after removal of the spleen, no hæmolysis takes place. In other words, hæmolysis occurs only in response to the introduction or production of hæmolysin in the presence of splenic and reticular tissue. The authors admit that a strict proof that the reticulo-epithelium is eliminated by blockage with iron granules cannot be adduced, but the conclusion appears to be justified that this procedure suffices to suppress its functions completely. In the animals treated with hæmolysin it has been possible to watch the appearance first of hæmoglobinuria and later of jaundice. They die within a short time and consequently the dissociation of the hæmoglobin usually does not reach the stage of bile pigment formation before death. When death is delayed for more than twenty-four hours, parenchymatous hæmorrhages appear in the liver and the lobules become tinted an orange yellow colour. Later the nuclei of the cells disappear and the cells themselves undergo complete disintegration.

Drs. Bieling and Isaac find that these changes are not the cause of the icterus. They suggest that these experiments together with others of an analogous character indicate that the process of hæmolysis in the body depends on the accumulation of damaged red blood corpuscles in the spleen and the solution of hæmoglobin. Part of the free hæmoglobin is transformed to methæmoglobin and appears in the urine unaltered. The remainder is transformed in the liver into bile pigments. They maintain that the spleen and the Kupffer cells take no part in the transformation. The same process probably is involved in the jaundice of paroxysmal hæmoglobinuria, hæmolytic jaundice and black water fever. As long as the liver parenchymatous cells are intact, free bile pigments will not flood the body. When they are damaged, jaundice appears.

[1] *Klinische Wochenschrift*, July 15, 1922.

Abstracts from Current Medical Literature.

SURGERY.

The Surgical Treatment of Pernicious Anæmia.

JAMES MORLEY HITZROT (*Annals of Surgery*, January, 1922) writes on the surgical treatment of pernicious anæmia. He classifies pernicious anæmia under two headings, the aplastic and the hæmolytic. In the former there is decreased blood formation. In the second there is increased blood destruction or at any rate blood destruction exceeds blood formation. The hæmolytic group contains two classes. In one the causative agent is known, as in the case of intestinal parasites; in the other it is unknown, as in Addison's pernicious anæmia. The aplastic anæmias occur chiefly in women before thirty and end fatally in a short time. Men are more often the victims of the other type. Barker considers that the blood picture upon which the diagnosis is based is indistinguishable in the Addison type from those of known origin in many cases. The forms of surgical treatment are blood transfusions, removal of foci of infection and splenectomy. Transfusion of human blood from a compatible donor is an established form of treatment. It may be done by the direct or by the citrate method. The quantity of blood transfused is not agreed upon. If the action of the introduced blood is to stimulate blood-forming organs, small quantities should be beneficial, but if it be to carry the patient along until those organs have had time to recover, large amounts would be necessary. Hitzrot states that repeated small or moderate transfusions have been as successful as large ones. In any case, transfusion acts as a temporary stay and does not cure the disease. The eradication of focal infection is now a popular therapeutic agent in pernicious anæmia. Infection of the gums and teeth receive particular attention, but the author says that the infective organisms should be proved to have a hæmolytic effect before concluding that they have a causal relationship to the disease. The results of splenectomy are not encouraging, especially in cases of disturbed blood formation, for the trouble does not lie in the spleen, but in the blood-forming organs. In the type showing increased blood destruction, many factors as yet undetermined must be solved before the therapeutic value of splenectomy can be settled. Hitzrot suggests that splenectomy should be considered in patients under forty-five who have an anæmia of the hæmolytic type with attacks of blood destruction (hæmatogenous crises) and periods of remission between the crises and also when the spleen is palpable. Splenectomy is contra-indicated in elderly people. Those who have splenectomy done early, seem to do better than those in whom it is done as a last resort.

Inguinal Herniotomy.

MARSH PITZMAN (*Annals of Surgery*, November, 1921) describes a fundamentally new technique for inguinal herniotomy. In discussing the anatomy of the inguinal canal he draws attention to the *ligamentum interfoveolare*, which runs from the inferior margin of the *transversus* muscle in front of the *fascia transversalis*, to be attached below to the inguinal ligament. Of all the operations performed for the relief of inguinal hernia, he thinks that Bassini's, as originally described, is the best, but unfortunately, he says, the performance is not as good as the description. He condemns the method of suturing the lower borders of the internal oblique and *transversus* muscles to the upper grooved surface of Poupart's ligament. Such sutures, in producing pressure necrosis of the muscle fibres, weaken the wall of the canal on the medial side of the abdominal inguinal ring and account for some of the occurrences which are prone to occur in this situation. The operation which he practises, differs from Bassini's in the fact that the internal oblique and *transversus* muscles are not sutured to the inguinal ligament, but are avoided carefully. While the sac is opened, mattress sutures are passed through the *fascia transversalis*, the neck of the sac and the upper surface of the inguinal ligament. He relies upon the co-aptation of the *fascia transversalis* and the inguinal ligament for the support of the canal. The cord is then placed in the canal and the external oblique tendon sutured and imbricated if necessary.

Carcinoma of the Rectum.

DANIEL FISKE JONES AND LELAND S. MCKITTRICK (*Annals of Surgery*, September, 1922) discuss the end results of operations for carcinoma of the rectum. The standard treatment of malignant disease, they point out, is excision of the growth with a wide margin of healthy tissue and as much of the lymph drainage area as possible. While this is admitted and practised in malignant disease of other parts of the body, some surgeons refuse to apply the principle to carcinoma of the rectum. Edwards is quoted as stating before the Royal Society of Medicine in 1911 that he could not agree with those who advocated the abdomino-perineal method any more than with those who for a limited carcinoma of the breast, would remove all but the ribs. F. T. Paul, in *The British Medical Journal*, 1912, asked why should an extensive excision of the mesentery be undertaken for the removal of glands which in all probability are not infected? The authors point out that, in spite of such opinions, there had been definite progress towards the more extensive operations until the last three or four years, when a retrograde tendency appeared. Herbert H. Brown in 1920 advocated the Kraske operation because a considerable proportion of the patients so operated upon by him during the last fifteen years were alive and well. Lockhart Mummery said he had given up the abdomino-perineal method, except in high carcinomata of the recto-sigmoid junction. Many surgeons claim that they can remove as much intestine by the posterior route as by the abdomino-perineal. This the authors admit, but they deny that it is possible to remove as much of the peri-rectal fat and mesentery by such an approach. In an analysis of several large groups of statistics up to 1915 they find that those who practised the posterior route, did not submit to operation more than 25% of the patients seen and of those surviving the operation only 16% lived three years, that is, of the patient met with, only 4% were alive three years later. In Harrison Cripps's series, which is the best recorded for the posterior route, only 9% of the total number seen survived for three years. Taking the results of the abdomino-perineal operation of Miles, 22.7% of the total number were alive at the end of three years. After considering the mode of spread of cancer of the rectum by permeation and lymphatic embolism, the authors conclude that, given a patient whose general condition will permit a severe operation, Miles's method is more likely to eradicate the disease than any other method.

Bone Grafts.

GEORGE DE TARNOWSKY (*Surgery, Gynecology and Obstetrics*, September, 1922), in an article entitled "Autogenous *versus* Heterogenous Bone Pegs," shows excellent results after the use of beef bone. In discussing the part played by bone grafts, whether autogenous or heterogenous, he concludes that the graft becomes absorbed by the penetration of vascular loops, but acts as a scaffold upon which grows new bone derived from the original bone of the part. If any part of an autogenous graft remains alive it is only small surface fragments which can derive enough nutriment from the tissue fluids in which they lie. He quotes Nathan, who, after describing how a growing bone of a young animal lengthens and thickens, says that "an implanted bone is absorbed but is more or less completely regenerated during the process. Bone dies when transplanted, whether supplied with periosteum or not." Gask also holds the opinion that the main mass of a bone graft dies. Hey Groves, while not so positive about the death and absorption of a bone graft, admits that dead bone in some cases gives as good results as living bone. He claims that this is shown by his experiment with a cat in which living and dead bone were transplanted into the right and left tibiæ respectively with identical results. The same surgeon is quoted further as having little faith in the osteogenetic power of periosteum. Tarnowsky uses grafts twelve and a half to fifteen centimetres (five to six inches) long and one and a quarter centimetres (half an inch) in diameter for fractures of the femur and for the tibia or humerus ten centimetres long and 0.8 centimetre in diameter. The

graft is taken from any of the long bones of a steer, denuded of periosteum and boiled for two hours on two consecutive days. It is then kept in a sterile container and boiled with the instruments when required for use.

GYNÆCOLOGY AND OBSTETRICS.

Fœtal Post-Maturity.

J. W. BALLANTYNE AND F. J. BROWNE (*The Journal of Obstetrics and Gynæcology of the British Empire*, Summer Number, 1922) have investigated the subject of fœtal post-maturity and the prolongation of pregnancy. They conclude that post-maturity of the fœtus has a real existence which may be recognized from the presence of a group of anatomical characters, such as excessive length, weight and ossification and easy separability of the *dura mater*, especially when these are associated with advanced senile changes in the placenta and cord. It is impossible to state with certainty the causes of fœtal post-maturity and the prolongation of pregnancy. The clinical evidence upon which the diagnosis of the latter condition is founded, consists of a number of data, none of which is absolutely free from fallacy; the most reliable is the determination of the size of the uterus made by a competent observer using the bimanual examination on several occasions from the second or third month onwards. Whilst the length of the menstruation-delivery interval and sometimes of the insemination-delivery interval can be ascertained, there is no means of calculating the impregnation-delivery period to within eight or ten days, which represents the maximum insemination-impregnation period. It is impossible therefore to state the exact duration of any pregnancy. At the same time, the establishment of the prolongation of pregnancy is a possibility and depends upon analogy with what is known to occur in the lower animals (*e.g.*, the cow) and upon several clinical details in history and symptomatology which, taken together, are sufficient proof. In medico-legal cases in which the medical evidence is conflicting, moral considerations often play a determining part. It is impossible to fix an upward limit to the duration of pregnancy; but the greater the deviation from the normal, the stronger must be the direct and collateral evidence. The dangers both to mother and child of a prolonged pregnancy are undoubted. They are chiefly associated with difficulty in the passage of the child and are greatly increased by reason of the unexpectedness of their emergence. Adequate ante-natal supervision provides a means by which the element of surprise can be eliminated from cases of post-mature labour, with immediate improvement in prognosis, both maternal and infantile. The treatment is prevention of prolongation of pregnancy by means of induction of labour at or soon after the carefully calculated full term of gestation. The authors recommend trial of the method by means of the administration of quinine, followed by pituitrin. They use two or three doses of 0.6 gramme (ten grains) of quinine to sensitize the uterus and give the pituitrin in repeated doses of 0.5 cubic centimetre with half-hour intervals. In one patient on whom this method was used, they had to administer chloroform on account of tetanic action of the uterus. In an appendix the authors give details of seventy instances of post-maturity which they have gathered from the literature. In these patients pregnancy is stated to have lasted from three hundred and five to three hundred and seventy two days.

Glycosuria in Pregnancy.

R. L. MACKENZIE WALLIS AND J. P. BOSE (*The Journal of Obstetrics and Gynæcology of the British Empire*, Summer Number, 1922) have reviewed the subject of glycosuria in pregnancy. They conclude that there are two types, an intermittent or transitory glycosuria and a severe glycosuria and true *diabetes mellitus*. The former shows certain characteristic features and may be diagnosed by means of blood and urinary analysis and the glucose tolerance test. The authors describe a new method of estimation of sugar in the urine in normal and abnormal amounts. By means of the glucose tolerance test it is possible to correlate the occurrence of intermittent glycosuria of pregnancy with hyper-activity of the pituitary body. The application of blood and urinary analysis to patients suffering from glycosuria of pregnancy renders it possible to differentiate between the two types. The importance of differential diagnosis is emphasized by the fact that the treatment of the two conditions is entirely different, the intermittent or transitory type requiring little if any dietetic treatment.

Pregnancy Following the Menopause.

M. L. BRANDT (*New York Medical Journal and Medical Record*, July 5, 1922) reports a case of pregnancy following the menopause. He points out that this is a very rare condition and gives references for the only five authentic cases that he can find in the literature on the subject. The case reported by him is that of a woman, forty-six years of age. She began to menstruate at thirteen. Menstruation was of the twenty-eight-day type and was always regular. She was married at eighteen and had eleven pregnancies with twelve children. The last labour occurred when the patient was thirty-nine years of age. Following this labour, menstruation occurred regularly for one year; the date of the last period was June, 1916. In March, 1919, she applied for treatment on account of the increasing size of her abdomen and intra-abdominal movements. In May, 1919, the patient was delivered of a male child weighing four kilograms (nine pounds). This child showed all the signs of achondroplasia. Ten months after the birth of the child the patient began to menstruate and had three normal periods. There has been no menstruation since that date.

Utero-Placental Apoplexy.

PRENTISS WILLSON (*Surgery, Gynecology and Obstetrics*, January, 1922), after reporting a case of utero-placental apoplexy and analysing sixty-eight cases in the literature, presents the following conclusions: Utero-placental apoplexy is caused by the inundation of the uterine wall with toxin of the nature of a hæmorrhagin, liberated from the placenta and, naturally, producing its maximum effect at the site of its observation and greatest concentration. Accidental hæmorrhage is probably in the majority of cases a manifestation of the same process. Clinically, the significant feature in the pathology is the damaged state of the uterine wall, which tends to cause intra-abdominal and *post partum* hæmorrhage. In severe cases, with an undilated cervix, the most conservative treatment is abdominal Cæsarean section, followed by hysterectomy, if necessary, in order to insure hæmatostasis.

The Harlequin Fœtus.

M. S. THOMSON AND C. P. G. WAKELEY (*Journal of Obstetrics and Gynæcology of the British Empire*, Summer Number, 1921) investigated two good specimens of the condition known as harlequin fœtus. They concluded that the harlequin fœtus is more closely allied to ichthyosis than to any other known condition. Histologically the two differ only in the relative widtn of the papillæ and inter-papillary ridges. The difference in the age incidence of the two is one of degree only and not of kind. It is the result of maternal hypo-thyreoidism coincident with an anomaly of the fœtal thyreoid gland which results in a decrease in its degree of activity. The explanation of the fact that this condition and true ichthyosis differ from cretinism lies in the existence of two isomers of thyreo-iodine.

Chorion Epithelioma of the Uterus.

H. E. MELENEY (*Surgery, Gynecology and Obstetrics*, August, 1922) reports a case of uterine chorion-epithelioma of the syncytial type which ended fatally. The *post mortem* examination showed a small tumour in the right cornu of the uterine cavity, acute infection of the endometrium extending through vessels about the right Fallopian tube, acute diffuse peritonitis and bacteriæmia due to *Streptococcus hæmolyticus*. The tumour consisted only of syncytial cells lying singly and in clumps in the swollen stroma of the uterine mucosa and in the superficial portion of the myometrium. The case illustrates the importance of early determination of the cause of uterine bleeding, not only in order to deal properly with the tumour itself, but also to avoid a termination by acute general infection.

British Medical Association News.

SCIENTIFIC.

A MEETING of the South Australian Branch of the British Medical Association was held in the Darling Building in the University of Adelaide on July 27, 1922, at the invitation of the Chancellor of the University. DR. T. G. WILSON, the President, was in the chair.

DR. W. T. HAYWARD, C.M.G., the Dean of the Faculty of Medicine, extended a cordial welcome to the members of the Branch. He stated that the Chancelolr of the University had had great pleasure in issuing invitations to the members of the South Australian Branch of the British Medical Association to hold a meeting in the Darling Building. He explained that it had been through the influence of some of the members of the Branch that they had been able to perpetuate the name of the Darling family in such an excellent manner. In conclusion, he congratulated Dr. T. G. Wilson on his occupancy of the Presidential Chair of the Branch.

DR. T. G. WILSON expressed the appreciation which the members felt of the kindness of the University authorities to invite them to the Darling Building.

The Work in the Laboratories.

PROFESSOR T. BRAILSFORD ROBERTSON explained the plan of the Darling Building and described in some detail the arrangement obtaining in the various departments. He referred to the principle of coordinating research work with teaching and pointed out that various departments were in a position to give valuable assistance to the medical profession within the State.

Professor Robertson proceeded to describe the work conducted in the biochemical laboratory in connexion with the diagnosis of various pathological conditions.

A series of demonstrations was held in the histological laboratory, in the physiological laboratory, in the biochemical laboratory, in the laboratory for advanced biochemistry, in the laboratory for advanced physiology, in the zoology museum, in the pathological museum and in the laboratory for advanced pathology.

A MEETING of the Victorian Branch of the British Medical Association was held at the Walter and Eliza Hall Institute of Research in Pathology and Medicine, Melbourne Hospital, on October 4, 1922, MR. G. A. SYME in the chair.

Splenomegaly.

DR. S. O. COWEN read a paper entitled "Familial Splenomegaly" (see page 545).

DR. H. DOUGLAS STEPHENS read a paper entitled "Clinical Symptoms of Enlargement of the Spleen in Children."

DR. S. W. PATTERSON read a paper written by MISS MAUD COWEN and himself entitled "Bile Salts in the Blood."

These papers and the discussion that ensued, will be published in THE MEDICAL JOURNAL OF AUSTRALIA of November 18, 1922.

A MEETING of the Western Australian Branch of the British Medical Association was held at the Children's Hospital, Perth, on October 18, 1922, DR. D. M. MCWHAE, C.M.G., C.B.E., in the absence of the President, in the chair.

Traumatic Lesions of the Knee Joint.

DR. F. GILL presented four children, all of whom had suffered some accidental injury to the knee joint.

The first patient was a male, aged seven years and seven months, who had run a nail into his knee joint on March 24, 1921. Within twelve hours the joint had become painful, swollen and hot. Two days later the child had been admitted to the Children's Hospital. The skin over the knee joint had been red, the joint swollen and hot. The temperature had been 38.8° C. (103° F.) and the pulse rate 116. The child had been anæsthetized and twenty cubic centimetres of pus had been aspirated from the joint. Six cubic centimetres of a 2% solution of formalin and glycerine had been injected. A splint had been applied. On the following day the aspiration and injection had been repeated and this had also been carried out on March 30, 1921. On April 4 the local and general condition had become worse. On the following day, that is, thirteen days after the accident, an operation had been performed. The joint had been exposed by two anterior and two posterior incisions and ten Carrel's tubes had been inserted. The limb had been placed in a Thomas's splint. A subcutaneous injection of three and a third litres of saline fluid had been given. On May 7, seven of the tubes had been removed, two antero-posterior and one transverse tubes remaining in place. On May 21 all the tubes had been removed and on June 21 the wounds had been healed. The child had eventually been discharged from hospital with an ankylosed knee joint.

The second child was nine years and eleven months. He had been struck on October 20, 1921, by a cricket ball on the knee. The knee had been painful for ten days. The boy had been admitted to hospital on November 1, 1921. At that time the knee was very swollen and painful and the appearance of the child was that of a toxic condition. The tongue was coated; the temperature was 38.3° C. (101° F.) and the pulse rate 126. The knee joint had been opened and had been found to be full of pus. After the pus had been removed, ten Carrel tubes had been inserted and a Thomas's splint applied. The child had spent four months in hospital, during which time the wound had healed except at one limited situation. During the following four months a few fragments of bone had separated and been discharged through the remaining sinus. On radiographic examination an area of rarefied bone had been seen in the centre of the lower end of the femur. In this there were some necrotic fragmnts. The wounds had ultimately healed and the patient had good movement of the joint.

The third patient was a girl, aged eight years, who had received a punctured wound over the knee joint by a pair of scissors on May 18, 1922. Immediately after the injury there was severe pain and swelling of the joint. She had been admitted to the hospital two days later, when her temperature was 38.3° C. and her pulse rate 98. The knee was held in a position of semi-flexion and was acutely tender. There was no fluid in the joint, but much swelling of the peri-articular tissues. Two days later fluid had been detected. On aspiration it had been found to be turbid. The joint had been washed freely with "Flavine" solution. During the following eight days there had been little pyrexia and the swelling of the joint had been much reduced. On June 4 the temperature had again risen and there had been a fresh increase of the swelling and pain of the knee joint. Pus had been aspirated on June 6 and the "Flavine" treatment repeated. The child's condition had not improved and consequently treatment by open operation had been adopted. Rectal injection of saline fluid and brandy by the mouth had been administered. On June 9 the wound had been dressed under an anæsthetic; it had looked quite clean and free from pus. After the removal of all the tubes on June 27 brilliant green had been used as an antiseptic. The wound was quite healed by the end of August.

The fourth patient was a boy who had received a blow on the knee joint on August 17, 1922. He had had a "cold" for two weeks. Three days later the knee had been found to be swollen and painful. The child's temperature had been 39.4° C. (103° F.). On August 23 he had been admitted to hospital looking very ill. There had been considerable swelling of the joint and great tenderness. After pus had been evacuated, an open operation had been performed. Ten tubes had been used. The joint had improved gradually under Carrel treatment and subsequently under icthyol and glycerine and brilliant green.

Still's Disease.

DR. D. M. MCWHAE, C.M.G., C.B.E., presented a patient, a boy, aged four and a half years, who had been seen for the first time as an out-patient at the age of two years. At that time there had been a fusiform swelling of the

inter-pharyngeal joints. Gradually other joints had become thickened and pulpy. The swelling had not been accompanied by effusion and no bone changes nor pain had been detected. Later the wrist, elbows, knees and ankles had become similarly affected. The lymphatic glands and the spleen had become enlarged. Nine months before admission a cough had occurred and a few rhonchi had been detected in the left lung. The lung had become solid and a septic form of pyrexia had developed. On percussion it had been found that the chest was dull, but no pus was detected by means of the hypodermic needle or by exploratory operation. Tubercle bacilli had been found in the sputum.

Dr. McWhae pointed out that the interest in the condition lay in the development of a tuberculous lesion in a patient who was suffering from an infection conforming in every respect with the disease described by Still. Poncet had described a condition as tuberculous pseudo-rheumatism with similar joint changes to those seen in the patient shown and had claimed that the lesion was due to a tuberculous toxin and not to tubercle bacilli. It had further been suggested that the real cause of Still's disease was the bacillus of tuberculosis. Dr. McWhae found that the evidence in favour of this view was not very good. In the majority of patients with Still's disease there were no manifestations of tuberculosis. The association of the two diseases in his patient, however, was of interest. He expressed the opinion that the tuberculous broncho-pneumonia was an intercurrent and terminal infection.

Congenital Ichthyosis.

DR. R. H. CRISP, the Chief Resident Medical Officer of the Children's Hospital, presented a series of patients on behalf of the members of the honorary medical staff.

The first patient was a girl, aged seven years, who had attacks of vomiting for two weeks and who had complained of toothache and constipation. It was found that the girl was affected with congenital ichthyosis. The family consisted of one boy and two girls. The patient's sister was affected to a less extent and her mother also had ichthyosis. The brother had a normal skin.

Hæmophilia.

A boy, aged five and a half years, had been in hospital for six weeks at the age of three years on account of severe hæmorrhage from a cut lip. It had been stated that he bruised easily. The patient's mother was dead. He had two sisters who were normal and two brothers who were bleeders. His knee, ankle, elbow and wrist joints had been enlarged from time to time. When the swelling occurred, the skin became red and shiny and the joints painful and tender. A little over six months before admission a swelling had appeared in the right calf, evidently a hæmorrhage. Subsequently a contracture of the foot—a *talipes equino-varus*—had developed. The patient had not been able to use the right leg effectively and it had become wasted. The tendon reflexes were almost normal. The faradic response was present, but all the electrical reactions were diminished as a result of the muscular wastage. The patient had an enlarged, narrow skull, with frontal bossing. The circumference of the skull was fifty-three centimetres.

Hydrocephalus.

A male child, aged nine years, was brought to the hospital on account of enuresis during the day and night time. The child had not had proper control of the bladder since birth. The action of the bowels was normal. It was noted that the child was small for his age and it was stated that his growth had been arrested. The lower extremities were well developed, while the upper extremities were badly developed and were capable of hyperextension. There was a marked squint. The birth had been prolonged, but had ended naturally. It had been noticed that the head was of peculiar shape. The fontanelles had been open at the age of two years. The child had been subject to attacks of vomiting since birth. The family history was unimportant. There was no serological evidence of syphilis. The circumference of the head measured fifty-two centimetres. The skiagram supported the diagnosis of hydrocephalus. The urine contained pus cells and casts and the bladder was distended.

Hemiplegia.

A child, aged nine years, was exhibited on account of cerebral palsy of the hemiplegic type. This child had been born precipitately into the chamber. It had not had any convulsions. Stiffness of the right arm and right leg had been noticed at the age of one year. He had commenced to walk at two. His serum had been tested by the Wassermann test and an incomplete reaction had been obtained.

Cardiac Œdema.

A male child, aged three years and three months, had been admitted to hospital with ascites and œdema of the legs. Three months before a brassy cough had been noticed, with wheezing and grunting respiration. These symptoms had varied in intensity and the child had become listless and disinclined to run about. One month before admission a swelling of the feet had appeared and the abdomen had become enlarged. On admission it had been found that the tongue was furred and the throat injected. The heart had been greatly dilated. The apex beat had been in the fifth interspace, five centimetres from the nipple line. The cardiac dulness had extended to the right sternal margin and upwards to the second interspace. No bruits had been detected. The rhythm had been rapid and of a galloping type. The volume of the pulse had been poor. There had been evidence of compression of the left lung, including a distant vesicular murmur and scattered rhonchi and râles. The abdomen had been greatly distended. The umbilicus had been everted. The lower edge of the liver had reached the level of the umbilicus. The spleen, however, had not been palpable. There had been much free fluid in the abdomen. There had been slight œdema of the legs and some purple, mottled spots had been seen on the arms and legs. The urine had been normal. No reaction had been obtained either to the Wassermann test or to the von Pirquet test. There had been no fever.

Empyema.

The next patient was a girl, aged two years and ten months, who had had morbilli and pneumonia one year previously. For three months prior to admission there had been cough which had been worse at night time and on awakening in the morning. There had been much offensive, thick yellow sputum, which at times was frothy. Just before admission a small quantity of blood had been detected. The child had been feverish at night. There was no tuberculosis in the family and the patient's father and mother, as well as the four other members of the family, were alive and well. On admission the patient had been found to be sallow and atonic. The breath had been foul. There had been deficient movement of the right side of the chest with falling in of the chest wall and dulness on percussion. Tubular breathing had been heard and many crepitant râles. There had been harsh, compensatory breathing in the left lung. The heart had not been displaced. The edge of the liver had reached to two finger's breadth below the costal margin. A blood count had revealed 15,000 leucocytes per cubic millimetre. No tubercle bacilli had been found in the sputum. An exploratory puncture had been carried out and pus evacuated. A rib had been resected and the patient had been treated with an autogenous vaccine.

Collapse of the Lung.

The patient, a girl, aged nine years and eight months, had been subject to attacks of bronchitis since infancy. She had not had rheumatic fever, nor had she been subject to sore throat, but had complained of "growing pains." The attack for which she had been admitted to hospital had commenced six weeks previously with coughing and the expectoration of yellow, inoffensive fluid. There had been a sore throat and a few follicular plugs had been seen on the tonsils. Later blood had appeared in the sputum and the child had been admitted to hospital. On examination it was found that the apex beat of the heart was in the fifth interspace, five centimetres outside the nipple line. The cardiac dulness extended to the right sternal border. Systolic and diastolic murmurs were heard at the apex. The greater part of the left side of the chest was dull to percussion; the dulness was more complete at the lower portion. Over the dull area there were no

movements of the chest wall. Occasional râles and bronchial breathing were heard in this region. Compensatory respiration of a harsh character was heard over the right lung. A very slight response to the von Pirquet test had been obtained. No tubercle bacilli had been found in the sputum. The temperature had occasionally risen to 37.8° C.. The diagnosis of collapsed lung was made.

Pyelitis.

The next patient was a girl, aged one year and two months. She had had symptoms for about five weeks which the parents had attributed to a fall on the head. During the two or three days prior to admission the child had become irritable and fretful and had retraction stiffness of the neck and vomiting had developed. There had been no symptoms of disturbance of the gastro-intestinal tract and the throat and chest had been found to be normal. After considerable difficulty a specimen of urine had been obtained. The urine had contained pus cells, a few red blood corpuscles and some bacteria. Improvement had occurred in response to treatment with alkalies.

Erythrœdema.

A female child, aged one year, had been admitted to hospital three weeks before the meeting on account of blepharo-spasm. An irritable macular rash had been seen in the skin of the buttocks and thighs. Marks of scratching and secondary infection had been present. The child had had an attack of gastritis six weeks before, but on admission there had been no diarrhœa. It had been very irritable and restless and had suffered from insomnia and photophobia. There was distinct hyper-extensibility of the joints, which remained in the position in which they were put. As a result, the child often assumed strange attitudes. There was a typical "raw beef" appearance of the hands and feet and some desquamation on the palms. The photophobia had been attributed to blepharitis of low degree. No definite pathological lesion had been discovered in the eyes. The condition was recognized as erythrœdema.

Otitis Media.

The last patient shown was a baby boy, aged ten months, who had started vomiting twelve days previously. It had been a healthy infant and had been brought up on the breast. The motions had been watery and contained curds. The child had been thirsty, irritable, drowsy and feverish. On admission some distension of the abdomen had been noticed. The ears had been examined and it had been found that the right *membrana tympani* was reddened and was bulging. An incision had been made and some pus evacuated. The general condition and the fever had not been greatly relieved. Examination had revealed the presence of albumin, blood and pus cells. It was held that the acute nephritis was secondary to the *otitis media*.

MEDICO-POLITICAL.

A MEETING of the Western Australian Branch of the British Medical Association was held at the Children's Hospital, Perth, on October 18, 1922, DR. D. M. MCWHAE, C.M.G., C.B.E., in the absence of the President, in the chair.

Extension of the Printing Arrangements of the Australasian Medical Publishing Company, Limited.

A letter addressed to the HONOURABLE DR. A. J. H. SAW, O.B.E., M.L.C., Director of the Australasian Medical Publishing Company, Limited, for Western Australia by the Secretary of the Company, dealing with the proposed extension of the printing arrangements of the Company, was read. It was intimated that the proposal involved the raising of ten thousand pounds sterling by the issue of debentures to the members of the several Branches. It was explained that the matter had been considered by the Council, who recommended it to the favourable consideration of the members. The acceptance of the proposal would mean that the members would be under an obligation to take up debentures to the extent of the quota for the State.

It was resolved to consider the matter at the next meeting of the Branch.

NOTICES.

THE COUNCIL OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION has arranged the following provisional programme of the Branch meetings. The Scientific Committee reserves to itself the right to modify the arrangements, but it is hoped that no changes will be necessary.

November 15, 1922.

CLINICAL MEETING at the Children's Hospital, Carlton, at 8.15 p.m..

NOMINATIONS AND ELECTIONS.

THE undermentioned have been elected members of the Victorian Branch of the British Medical Association:

ALEXANDER, JAMES BUCHANAN, M.B., B.S., 1922 (Univ. Melbourne), 17, Glendearg Grove, Malvern.

BUZZARD, IRVING, M.B., B.S., 1922 (Univ. Melbourne), "Norwood," Glenhuntly Road, South St. Kilda.

GREEN, RICHARD THOMAS BONFIELD, M.B., B.S., 1922 (Univ. Melbourne), 20, Florence Road, Surrey Hills.

HARRIS, THOMAS ALEXANDER BRITTEN, M.B., B.S., 1922 (Univ. Melbourne), 595, Burke Road, Camberwell.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held on August 4, 1922, at the University of Adelaide.

Polar Cataract.

DR. R. H. PULLEINE referred to a patient shown at a previous meeting by Dr. F. H. Beare. The patient has a bilateral anterior polar cataract. He stated that anterior polar cataract could arise in two ways. It could be congenital or acquired. Congenital polar cataract was due to the imperfect closure of the lens vesicle. The acquired form might arise from ulceration of the cornea shortly after birth. The ulceration might be central or paracentral. As a result of the ulceration the aqueous fluid in the anterior chamber escaped and the posterior surface of the cornea came into contact with the anterior surface of the lens. When the ulceration healed, the anterior chamber was again closed. As the corneal ulceration disappeared, a small opacity forming the anterior polar cataract remained. At times the cornea remained adherent to the anterior surface of the lens by means of a small filament or even by a pyramidal projection from the lens.

Posterior polar cataract occurred as a congenital condition. There were two varieties, the *vera* and the *spuria*. The former consisted of an opacity at the posterior pole of the lens. Its genesis was not understood. The latter type was due to failure of the hyaloid artery to disappear. When anterior and posterior cataract occurred at the same time, the condition was spoken of as fusiform cataract.

DR. W. RAY drew attention to the frequency with which opacity of the lens occurred in diabetes. He raised the question whether the opacity might not be due to an alteration of the physical condition of the colloids in the lens as a result of an alteration of reaction. In all cataracts drops of oily material were frequently found, as well as deposits of cholesterol. He claimed that this pointed to a disturbance of the equilibrium of the colloids and emulsions in the lens.

DR. C. T. TURNER said that he had seen a patient with diabetes in whom an opacity of the lens had developed without any signs of acidosis.

DR. A. A. LENDON AND DR. R. H. PULLEINE had seen cataract in both thin and fat persons suffering from diabetes. The latter referred to the alleged high incidence

of cataract in India. It had been suggested that it was the result of defective nutrition.

SIR JOSEPH VERCO thought that, although the number of cataracts in India might be very large, the incidence of the affection might be no greater than in other communities.

PROFESSOR J. B. CLELAND said that rheumatoid arthritis had been attributed to an imperfect supply of nutrients in the synovial fluid, with consequent degeneration of the cartilage cells. He suggested that the changes in the lens in cataract might have a similar origin. He raised the question whether cataract was commoner in blue or in dark eyes.

DR. HELEN MAYO stated that the majority of Indians had dark eyes.

DR. PULLEINE said that cataract was rare in Australia. It would thus appear that intensity of sunlight had little to do with its origin.

PROFESSOR T. BRAILSFORD ROBERTSON stated that in his experience exposure of mice to ultra-violet light for periods sufficiently long to cause intense sunburn in shaven portions of the skin did not appear to cause any injury to the eye.

PROFESSOR CLELAND said that in epithelioma of the breast very long cells with the nucleus at one end, grouped in arcuate masses, were sometimes found. He suggested that the lens might originate in a manner similar to the growth of these masses.

Hæmoglobin Content and Volume of the Blood.

DR. L. B. BULL gave a report of work recently carried out at the Adelaide Hospital on the standardization of Sahli's hæmoglobinometer by Barcroft's oxygen capacity method. A very close agreement between the two methods had been obtained, but the incidental observation had been made that the hæmoglobin content of blood drawn from the finger was invariably higher than that of blood obtained from veins. The variation between the two was not constant, but some degree of deviation was nearly always present.

PROFESSOR T. BRAILSFORD ROBERTSON referred to the recent work of Whipple and Delprat. These observers had found that blood volume estimated from plasma volume and the ratio of corpuscles to plasma measured by the hæmatocrit was lower than the blood volume computed by the addition of separate estimates of the plasma volume and corpusclar volume. They had inferred that the difference was due to a relative increase of the volume of corpuscles in the capillary bed. They had thus been enabled to estimate the volume of these relatively immobilized corpuscles.

DR. W. RAY spoke of the work of Dreyer and Ray, in which it had been shown that washing out the blood vessels for twenty-four to thirty-six hours with Ringer's solution did not suffice to release all the corpuscles contained in the capillaries.

Blood Grouping.

DR. D. L. BARLOW gave an account of the results obtained in the determination of the grouping of the blood of newborn infants. The blood had been obtained from the umbilical cord vein. The blood of forty infants had been tested in this way. In about two-thirds it had been possible to determine the group to which the blood belonged. Typical reactions of the corpuscles and serum had been observed. In the remaining third the corpuscles were agglutinable, but the serum did not possess the power of inducing agglutination.

The serum of persons whose blood belonged to Group IV., agglutinated corpuscles of Group II. more rapidly than those of Group III.. It seemed as if the power of agglutination of one type of corpuscle developed more rapidly than that of another. The hæmolysing power of these sera was inferior to their agglutinating power. It was distinctly less than that of blood of adults. Little, if any, hæmolysing power was evidenced.

DR. H. K. FRY asked whether jaundice in new-born infants might not be due to hæmolysis. Dr. Barlow's results appeared to render this unlikely.

The question was raised as to whether the fatal results occasionally following transfusion of blood were due primarily to hæmolysis or agglutination.

DR. C. T. TURNER stated that hæmoglobin appeared in the urine during the first twenty-four to forty-eight hours after transfusion in many instances, but was not associated with blood corpuscles. As soon as the hæmoglobin disappeared, the patients got well. In the fatal cases sudden death occurred during the transfusion. He assumed that the corpuscles of the donor agglutinated and a clot was formed running back from the vein in the arm into the superior *vena cava* and the right side of the heart.

DR. W. RAY spoke of the occurrence of albuminuria which occurred after auto-transfusion of laked blood. The animals died within a very short time. In rabbits there was an almost complete denudation of the epithelium of the renal tubules. The picture of a fulminating nephritis was obtained. The epithelium from the tubules appeared as casts and the urine was loaded with hæmoglobin and albumin. No intravascular clotting took place.

DR. C. T. TURNER pointed out that when transfusion was carried out with the blood of "universal" donors, no untoward results occurred. The results he had described arose when blood from a donor did not belong to the "universal" group or to the group corresponding to the recipient's blood.

Post-Graduate Work.

POST-GRADUATE COURSE IN SYDNEY.

WE have been asked to announce that arrangements have been made to hold the post-graduate course in Sydney from January 8 to Janury 19, 1923. The programme is being compiled by the Sydney University Extension Board.

The lectures and demonstrations will be given at the Royal Prince Alfred Hospital, the Sydney Hospital, the Royal Hospital for Women, Paddington, the Royal Alexandra Hospital for Children, the Coast Hospital and the Medical School.

The following is a list of subjects that will be dealt with: Cardiac disease, renal disease, glycosuria, the physiological aspects of respiration in relation to clinical work, functional digestive disease, the surgery of the gall bladder, the bile ducts and the stomach, diseases of the eye, ear, nose and throat, pitfalls of gynæcology, indications for obstetrical operations, rheumatic heart affections in children, infant feeding, abdominal emergencies in children, infectious diseases, nervous diseases in children, skin diseases in children, the medical aspect of life insurance, radiography, fractures and orthopædic methods, *inter alia*.

The fee for the course is three guineas. Applications to join the course should be addressed to I. G. MACKAY, ESQUIRE, B.A., C.M.G., D.S.O., Secretary of the University Extension Board, University of Sydney, Newtown.

A complete programme will be published at a later date.

Obituary.

JOHN HIGGINS.

WE regret to announce the death of Dr. John Higgins, of Clermont, Queensland, which took place on October 25, 1922.

HENRY FRANCIS SADLER.

WE regret to announce the death of Dr. Henry Francis Sadler, of Parkes, New South Wales, which took place at a private hospital in Sydney on October 23, 1922,

Naval and Military.

APPOINTMENTS.

THE following appointments, promotions, etc., have been announced in the *Commonwealth of Australia Gazette*, Nos. 81 and 83, of October 5 and 12, 1922:

Permanent Naval Forces of the Commonwealth (Sea-Going).

THE GOVERNOR-GENERAL IN COUNCIL has approved of the services of SURGEON-LIEUTENANT JOHN HERBERT BLACKBURN in the Permanent Naval Forces of the Commonwealth (Sea-Going) being dispensed with, under Section 30 of the *Naval Defence Act, 1910-1918*. Dated 11th October, 1922.

Australian Military Forces.

SECOND MILITARY DISTRICT.

First Cavalry Division: Staff.

MAJOR R. W. W. WALSH, D.S.O., relinquishes the appointment of Deputy Assistant Director of Medical Services, Divisional Head-Quarters, 30th June, 1922.

First Division: Staff.

MAJOR W. VICKERS, D.S.O., relinquishes the appointment of Deputy Assistant Director of Medical Services, Divisional Head-Quarters, 30th June, 1922.

Second Division: Staff.

CAPTAIN AND BREVET-MAJOR (TEMPORARY MAJOR) G. C. WILLCOCKS, O.B.E., M.C., relinquishes the appointment of Deputy Assistant Director of Medical Services, Divisional Head-Quarters, and the temporary rank of Major, 30th June, 1922.

Australian Army Medical Corps.

LIEUTENANT-COLONEL (provisionally) A. J. MACKENZIE to be supernumerary to the establishment of Lieutenant-Colonels, with pay and allowances of Major, 1st July, 1922.

MAJOR (HONORARY LIEUTENANT-COLONEL) L. W. BOND, D.S.O., and MAJORS F. L. BIGNELL, D.S.O., C. L. CHAPMAN, D.S.O., G. C. BYRNE, D.S.O., C. L. S. MACINTOSH, D.S.O., and W. E. KAY, D.S.O., to be supernumerary to the establishment of Majors, with pay and allowances of Captain, 1st July, 1922.

LIEUTENANT-COLONEL (provisionally) J. J. HOLLYWOOD relinquished the command of the First Field Ambulance, 30th June, 1922.

LIEUTENANT-COLONEL A. L. DAWSON, D.S.O., relinquished the command of the Fourth Cavalry Field Ambulance, 31st July, 1922, and is transferred to the Reserve of Officers, 1st September, 1922.

MAJOR E. M. RAMSDEN is transferred to the Reserve of Officers, 1st September, 1922.

MAJORS W. T. NEWTON and L. COWLISHAW are transferred to the Reserve of Officers, 1st July, 1922.

CAPTAINS (HONORARY MAJORS) J. M. ALCORN and E. A. SANBROOK and CAPTAINS J. A. JAMES, W. F. MATTHEWS, J. MCPHERSON, H. H. WILLIS and E. K. PARRY, M.C., are transferred to the Reserve of Officers and to be Majors, 1st July, 1922.

CAPTAIN (HONORARY MAJOR) N. M. A. ALEXANDER and CAPTAINS W. W. MARTIN, C. ANDERSON, M.C., H. G. LEAHY, E. W. B. WOODS, M.C., E. E. PITTMAN, R. J. HUNTER, A. M. ASPINALL, L. T. ALLSOP, M.C., T. E. PARKER and W. K. W. FLOOK and LIEUTENANT L. J. SCOTT are transferred to the Reserve of Officers, 1st July, 1922.

CAPTAINS (provisionally) F. R. CUMMING, R. V. GRAHAM and O. E. J. MURPHY and LIEUTENANT (provisionally) E. ROSANOVE are transferred to the Australian Army Medical Corps Reserve and to be Honorary Captains, 1st July, 1922.

LIEUTENANTS (provisionally) D. B. LOUDON, W. J. CHAPMAN, F. A. E. LAWES, H. W. T. CHENHALL, M. B. FRASER and J. I. HUNTER are transferred to the Australian Army Medical Corps Reserve and to be Honorary Lieutenants, 1st July, 1922.

THE resignation of LIEUTENANT G. B. WHITE of his provisional appointment is accepted, 30th June, 1922.

THIRD MILITARY DISTRICT.

Australian Army Medical Corps.

To be Quartermaster and Honorary Major—MAJOR R. A. LOWRY, from the Reserve of Officers, with pay and allowances of Captain, 1st July, 1922.

LIEUTENANT (provisionally) C. E. V. SUTHERLAND is transferred to the Australian Army Medical Corps Reserve and to be Honorary Lieutenant, 1st July, 1922.

Australian Army Medical Corps Reserve.

LIEUTENANT (provisionally) L. G. MALE is transferred from the Australian Army Medical Corps, Fifth Military District, and to be Honorary Captain, 1st July, 1922.

FIFTH MILITARY DISTRICT.

Australian Army Medical Corps.

LIEUTENANT (provisionally) L. G. MALE is transferred to the Australian Army Medical Corps Reserve, Third Military District, and to be Honorary Captain, 1st July, 1922.

Special Correspondence.

LONDON LETTER.

BY OUR SPECIAL CORRESPONDENT.

The Variola Outbreak.

AT the time of my writing the outbreak of small-pox in London has caused four deaths among the ten patients whose infections have been detected. The group of cases appears to furnish on analysis several points having epidemiological and clinical interest. Within a few days one case of small-pox was notified in each of two boroughs in Central London and one in Southend, thirty-eight miles from Charing Cross. The last named patient, who was having his holiday, lived when at home in one of the mean streets of the densely populated area lying near the junction of the city with the East End; and one of the other patients had had business transactions in the same area. Inquiries in this street, made some time later, were for a time fruitless, but a barber reported having refused a few weeks earlier, to cut the hair of a boy whom he found to have spots in his scalp. This boy, on examination by the Public Health staff, proved to have scars distributed in a manner characteristic of small-pox and was found to have had, some weeks ago, a conversation in the street with the patient who was taken ill in Southend; fourteen days later the rash had appeared in the latter person. This boy assisted his mother in the business of a small shop, at which two of the patients detected later were found to have bought goods. One woman whose connexion with this infection was no more close than that of passing through the neighbourhood daily on her way to work, developed small-pox and died. In one industrial borough in the East End five persons contracted small-pox, of whom one had dealt at the shop already mentioned and the remainder owed their infection to this one.

At the moment, fourteen days have elapsed since the detection of the last case and there is much ground for hoping that vigorous pursuit and isolation of the contacts has checked the spread of infection. The outbreak has showed, however, a striking alternation of mild with severe cases and it is still possible that persons with undetected mild illness are infecting other persons, whose illness will commence towards the end of the ensuing fortnight. Examining the diagnostic difficulties to which these cases have led, one finds that the classical confusions

with measles and chicken-pox respectively have been well represented. One adult female was operated on for appendicitis in one of the largest general hospitals. She showed subsequently a rash regarded as German measles and within four days had to be removed to the small-pox isolation hospital. This patient suffered from the disease in its confluent form. Two patients were sent home from out-patient hospital departments, having been told that they were suffering from chicken-pox. Two were detected during visits of inquiry by the sanitary inspector and had not had medical treatment. One patient had a prodromal rash which was notified as scarlet fever. From the last and more extensive London outbreak an example may be recalled which emphasizes the grave difficulties which beset even competent and experienced observers in connexion with the diagnosis of small-pox. After several attendances at the out-patient dermatological clinic of a large general hospital a patient was recommended for admission to the local poor law infirmary, where, the diagnosis of septic dermatitis being still accepted, he was treated for many days. It was not until two members of the staff contracted small-pox in a severe form that the true nature of his complaint was recognized.

At the present time small-pox in England is practically confined to the London, Nottingham and Middlesborough districts. In each of the latter about a hundred cases have been reported during a period of several months and sporadic cases are still being encountered in the vicinity. Southampton has also had one or two cases. It is believed by many that a serious and wide-spread epidemic of small-pox is bound to occur before long. The proportion of exemptions (secured on so-called "conscientious" grounds) from infant vaccination is steadily rising, so that it has been calculated that fewer than 50% of children are now vaccinated; in many areas the proportion is still smaller. I am told that the objection to infant vaccination is now found in many cases to be more serious on the paternal than the maternal side and I have heard it suggested, possibly with some degree of truth, that the present-day fathers' experiences of inoculation during military life have produced in many of them a regrettable but obstinate antipathy to inoculation of their children by lymph vaccine.

Correspondence.

HEXAMETHYLENE-TETRAMINE IN PYELITIS.

SIR: As a general country practitioner who is accustomed to follow in treatment the views of specialists as expressed in your columns, I would like to make sure that those of Dr. Gifford Croll are generally accepted before reversing what have been my usual therapeutic procedure.

In an article headed "Urinary Infection in Children," read at a meeting of the Queensland Branch on September 1 and appearing in THE MEDICAL JOURNAL OF AUSTRALIA of October 14, Dr. Croll states, in referring to the treatment of infantile pyelitis, that he "usually gives six decigrammes of potassium citrate every two hours . . . and finally three times a day when the urine has become alkaline." I have found this treatment particularly effective in the presence of bacilluria of the same type.

The author then goes on to state: "If this is not effective, I add 'Urotropine' or 'Hexamine'" and, again: "I do not know which is the better, 'Urotropine' or 'Hexamine'; I find them both effective, even in an acid urine."

I have always been under the impression that "Urotropine" or "Hexamine" should only be demonstrated in an acid urine; that they are only effective as urinary antiseptics and that their therapeutic efficiency is nullified in the presence of an alkaline urine.

In the latest edition of Squire (page 694) it is stated that "it ('Hexamine') should never be given with potassium citrate." . . . A quotation from *The British Medical Journal* of 1913.

On the same page *The Lancet* is also quoted to the effect that "'Hexamine' should not be given with drugs such as potassium citrate in sufficient quantity to produce an alkaline urine."

I do not wish to be merely argumentive, but the authorities quoted are in marked variance.

When Dr. Croll states that "he finds them both effective, even in acid urine," he must regard them as more likely to be effective in an alkaline urine than an acid one.

As the therapeutic principle involved has an important practical bearing, I think the position needs, like the bacilluria itself, a little clarification.

Yours, etc.,

A. W. ST. LEDGER, M.B., B.S..

Cunnamulla, Queensland,
October 21, 1922.

THE DEMONSTRATION OF THE SPIROCHÆTA PALLIDA IN PRIMARY SORES.

SIR: The dark ground illumination method is now so universally in use in pathological laboratories that the following note may be of interest:

A short time ago my dark ground apparatus was accidentally damaged beyond repair. In despair, almost, I resorted to what I was taught fifteen years ago by Professor Arning at Hamburg, namely, the staining of fibres, a method which I, on account of the dark ground method, had not again made use of.

To my astonishment I now find that the staining method is in every way so superior to the dark ground method that I have totally discarded the latter. But, apart from this the stained film method makes it so easy for the practitioners to forward specimens for examination that I have no hesitation in giving some detail as to how slides are prepared.

The sore must have had no dressing for at least thirty-six hours. Wash the sore with water; apply some wool soaked in methylated spirit for not less than one minute; wash again with water. Scrape the sore, very superficially, until there is a slight oozing of serum and blood. Transfer a small drop on to a slide; spread it out thinly and allow to dry; do not fix by heat.

Yours, etc.,

ALFRED E. FINCKH.

The Sydney Clinical Research Laboratories,
26, College Street, Sydney,
November 1, 1922.

THE TREATMENT OF TALIPES EQUINO-CAVUS.

SIR: In the report of the Pædiatric Society, Melbourne, dealing with the above case, it is stated that the child was "put up in plaster for three weeks." It should have been: "put up in a splint for three days." Early walking, even at the risk of breaking down the wound, is the most important detail in the after-treatment.

Yours, etc.,

W. KENT HUGHES.

22, Collins Street, Melbourne,
November 3, 1922.

CONGRESS OF THE FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE.

AT the Fourth Congress of the Far Eastern Association of Tropical Medicine, held at Weltevreden, Java, in August, 1921, a proposal was made on behalf of the Governments of the Straits Settlements and Federated Malay States by their delegate, Dr. A. E. Horn, that the next meeting of the Association be held in Malaya.

The laws of the Association provide that the meetings shall be held every two years and, as the proposal was accepted, the Congress will meet in Malaya in 1923.

Dr. A. E. Horn was chosen President for the forthcoming session.

Dr. A. L. Hoops and Dr. R. Dowden were elected as

Vice-Presidents for the Straits Settlements and Federated Malaya States respectively and Dr. Scharff as Honorary Secretary for Malaya.

On April 21, 1922, a meeting was held to elect committees for the organization of the Congress. Subsequently other meetings were held and definite schemes were prepared for the management of Congress. It has been decided to hold the meeting from September 3 to September 17, 1923. The first week of this period will be devoted to scientific discussions and the following week to excursions to points of medical and sanitary interest throughout Malaya.

The Governments of the Straits Settlements and Federated Malay States have recognized the important functions of this Association and are contributing a considerable sum towards the expenses.

The object of this Association is to promote the science and art of tropical medicine in the Far East. For this purpose the Association endeavours to unite into one compact organization the medical profession of the Far East, for the growth and diffusion of medical knowledge, to promote friendly international intercourse among physicians, to elevate the standard of medical education, to enlighten and direct public opinion in regard to the problems of hygiene, to form habits which may conduce to the prevention of disease among the native population and to present to the world the results of such scientific observations.

The membership of this Association consists of the members of all duly constituted, regularly organized medical societies within the field of this organization and all medical officials in the civil, military, naval or other organized services of Governments within their territories.

It is requested that those who wish to submit papers, will communicate with the Honorary Secretary as soon as possible.

Books Received.

ENCYCLOPÆDIA MEDICA, under the General Editorship of J. W. Ballantyne, M.D., C.M., F.R.C.P.E.; Second Edition; Volume VIII., Labyrinth to Mammary Gland; 1922. Edinburgh and London: W. Green & Son, Limited; Sydney: Butterworth & Company (Australia), Limited; Royal 8vo., pp. x. + 704. Price: 20s. net.

THE ANATOMY OF THE FEMALE PELVIS, DESCRIPTIVE AND APPLIED, by F. A. Maguire, D.S.O., M.B., Ch.M. (Syd.), F.R.C.S. (Eng.); 1922. Sydney: Angus & Robertson, Limited; Crown 8vo., pp. 115, with four illustrations. Price: 6s. net.

Medical Appointments.

DR. H. HUFF JOHNSTON (B.M.A.) has been appointed Honorary Ear, Nose and Throat Surgeon to the Coast Hospital, New South Wales.

* * * *

DR. R. P. MCMEEKIN and DR. F. W. STONE (B.M.A.) have been appointed under the *Workers' Compensation Act, 1915*, of Victoria Certifying Medical Practitioners and Medical Referees at Melbourne.

Medical Appointments Vacant, etc.

FOR announcements of medical appointments vacant, assistants, *locum tententes* sought, etc., see "Advertiser," page xviii..

DEPARTMENT OF PUBLIC HEALTH, NEW SOUTH WALES: Third Government Medical Officer.

LADY BOWEN LYING-IN HOSPITAL, BRISBANE: Assistant Honorary Physician in Charge of the Ante-Natal Department.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, 429, Strand, London, W.C..

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney	Australian Natives' Association Ashfield and District Friendly Societies' Dispensary Balmain United Friendly Societies' Dispensary Friendly Societies Lodges at Casino Leichhardt and Petersham Dispensary Manchester Unity Oddfellows' Medical Institute, Elizabeth Street, Sydney Marrickville United Friendly Societies' Dispensary North Sydney United Friendly Societies People's Prudential Benefit Society Phœnix Mutual Provident Society
VICTORIA: Honorary Secretary, Medical Society Hall, East Melbourne	All Institutes or Medical Dispensaries Australian Prudential Association Proprietary, Limited Manchester Unity Independent Order of Oddfellows Mutual National Provident Club National Provident Association
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane	Brisbane United Friendly Society Institute Stannary Hills Hospital
SOUTH AUSTRALIA: Honorary Secretary, 12, North Terrace, Adelaide	Contract Practice Appointments at Renmark Contract Practice Appointments in South Australia
WESTERN AUSTRALIA: Honorary Secretary, Saint George's Terrace, Perth	All Contract Practice Appointments in Western Australia
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington	Friendly Society Lodges, Wellington, New Zealand

Diary for the Month.

Nov. 14.—New South Wales Branch, B.M.A.: Ethics Committee.
Nov. 15.—Victorian Branch, B.M.A., and Melbourne Pædiatric Society: Joint Meeting.
Nov. 15.—Western Australian Branch, B.M.A.: Branch.
Nov. 16.—Victorian Branch, B.M.A.: Council; Nomination of London Representative.
Nov. 16.—North-Eastern Medical Association, New South Wales.
Nov. 15.—Victorian Branch, B.M.A.: Branch.
Nov. 21.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Nov. 21.—Illawarra Suburbs Medical Association, New South Wales: Annual Meeting.
Nov. 23.—Brisbane Hospital for Sick Children: Clinical Meeting.
Nov. 24.—New South Wales Branch, B.M.A.: Branch.
Nov. 24.—Queensland Branch, B.M.A.: Council.
Nov. 28.—New South Wales Branch, B.M.A.: Medical Politics Committee; Organization and Science Committee.
Nov. 28.—Victorian Branch, B.M.A.: Ballot Paper Issued.
Nov. 29.—Victorian Branch, B.M.A.: Council.
Nov. 30.—South Australian Branch, B.M.A.: Branch.
Dec. 1.—Queensland Branch, B.M.A.: Branch.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, B.M.A. Building, 30-34, Elizabeth Street, Sydney. (Telephone: B. 4635.)

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